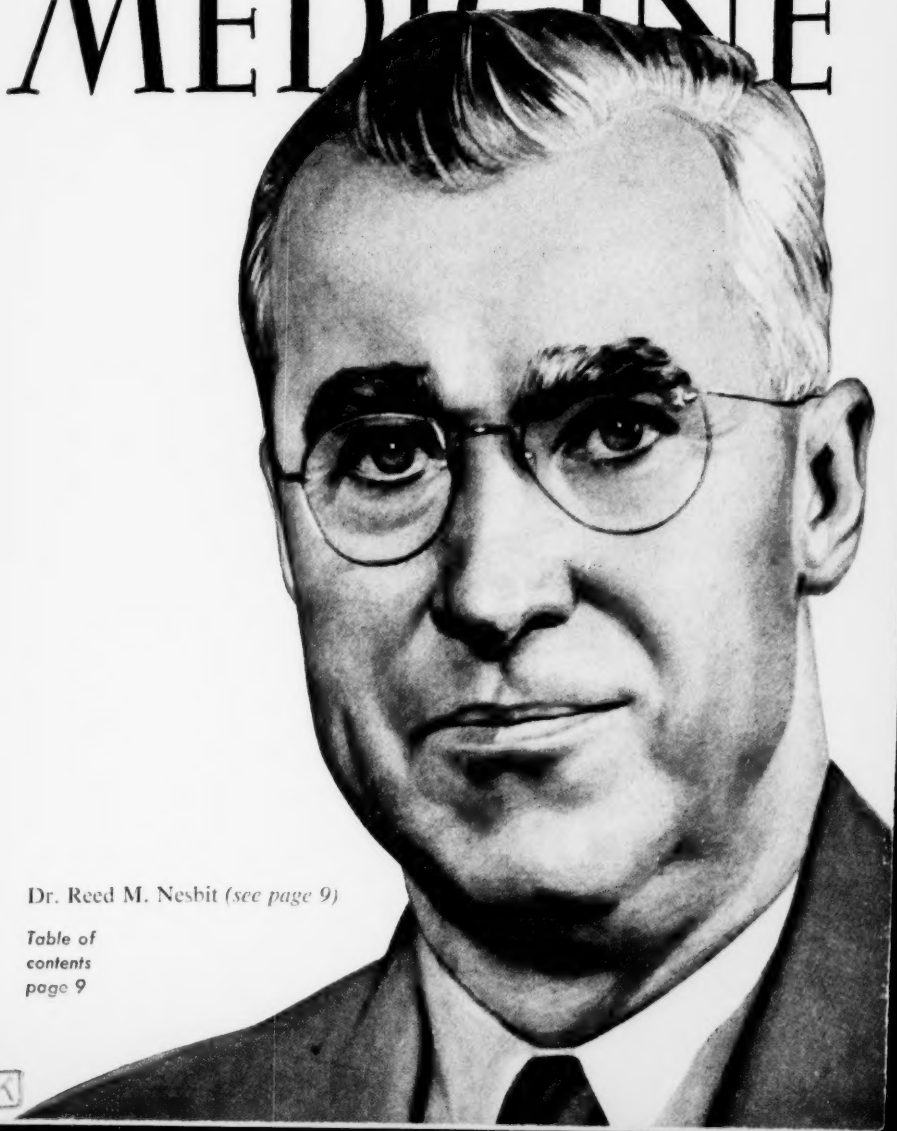
MARCH 15, 1953

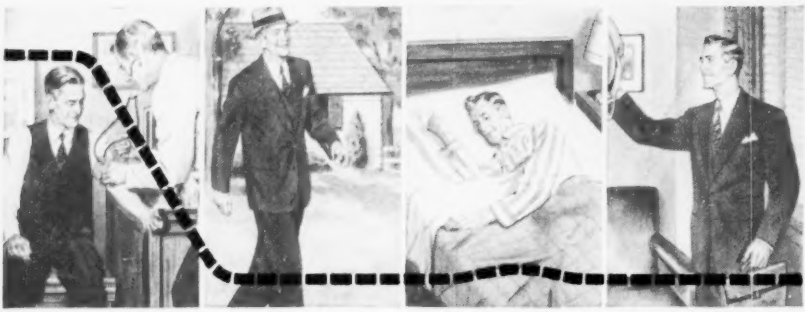
MODERN MEDICINE

The Journal of Diagnosis and Treatment



Dr. Reed M. Nesbit *(see page 9)*

Isn't this the picture you want to prescribe for your hypertensive patients?



Nitranitol's safe, gradual, prolonged vasodilation permits hypertensives to resume more normal lives.

And . . . therapeutic dosages of NITRANITOL can be maintained over long periods of time . . . *without* frequent checkups . . . *without* worry about possible toxic effects.

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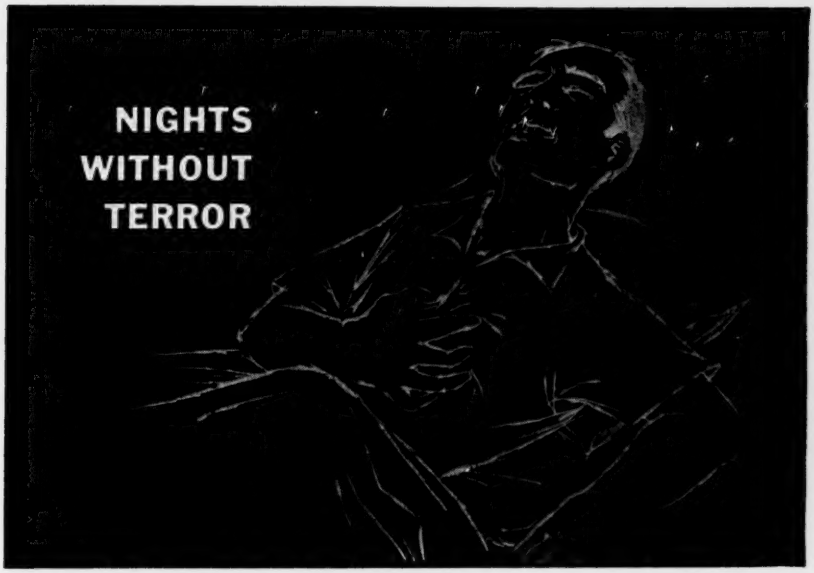

to prevent attacks in angina pectoris

Nocturnal angina pectoris (as well as day-time attacks) responds gratifyingly to Peritrate. Investigators report that in patients on Peritrate "insomnia due to pain was much reduced and they were able to enjoy reasonably good sleep."[1] Others had less palpitation during the night "and were able to sleep on the left side" which they had been unable to do prior to Peritrate.[2] When required, an extra 1-1½ tablets taken on retiring brought "striking relief."[1]

Prophylactic Management

Peritrate—a long-lasting coronary vasodilator—prevents rather than relieves attacks. The prophylactic action of each dose lasts 4 to 5 hours. One to 2 tablets of Peritrate, taken 3 to 4 times daily, can . . .

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Effective in 4 out of 5 Patients

Fewer or less severe attacks occurred in 80% and 78.4% of patients,[1,2] and in the majority the need for nitroglycerin was reduced. Clinical improvement has been verified by EKG findings and exercise tolerance may improve measurably.[2,3]

Available in 10 mg. tablets in bottles of 100, 500 and 5000.

Literature and samples on request.

1. Humphreys, P., et al.: Angiology 3:1 (Feb.) 1952.
2. Plotz, M.: New York State J. Med. 52:2012 (Aug. 15) 1952.
3. Perlman, A.: Angiology 3:16 (Feb.) 1952.

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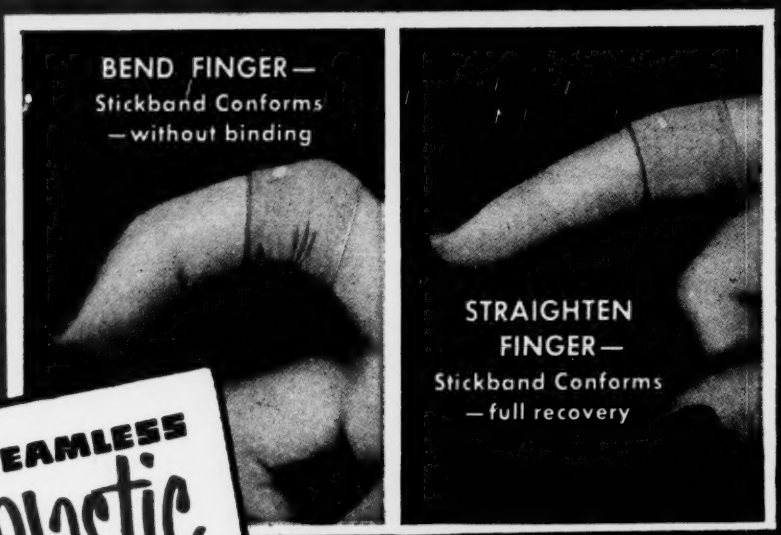

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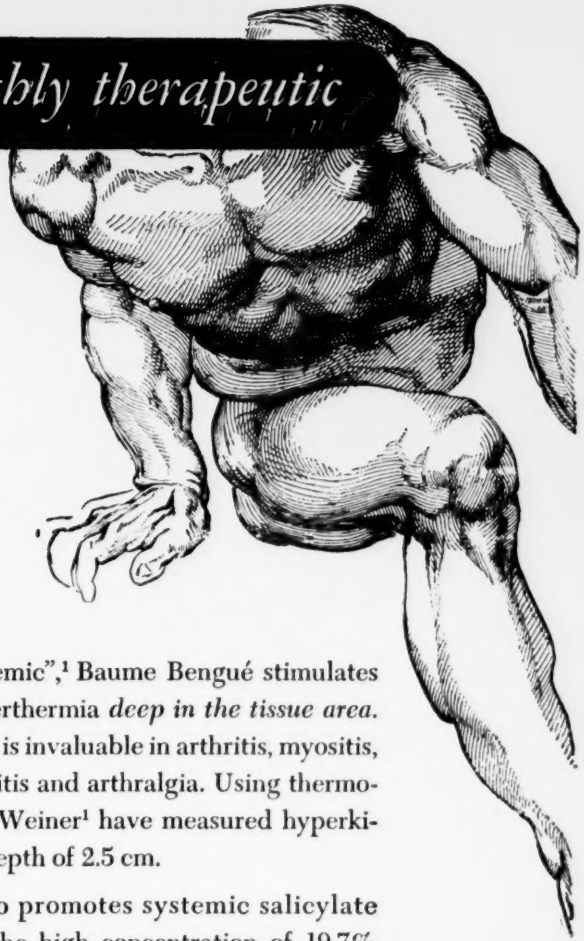

As a true "hyperkinemic",[1] Baume Bengué stimulates hyperemia and hyperthermia *deep in the tissue area.* This thorough action is invaluable in arthritis, myositis, muscle sprains, bursitis and arthralgia. Using thermoneedles, Lange and Weiner[1] have measured hyperkinemic activity at a depth of 2.5 cm.

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1. Lange, K., and Weiner, D.: J. Invest. Dermat. 12:263 (May) 1949.

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THE JOURNAL OF DIAGNOSIS AND TREATMENT

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Also available with ½ gr. phenobarbital

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MODERN MEDICINE
THE JOURNAL OF DIAGNOSIS AND TREATMENT

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[illegible] A. D. Jr. Med. Clin. North Amer. 36:1607, Nov. 1952

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that stay fresh

No more need to worry about shelf deterioration of vitamins for little tots. The packaging of 'Vi-Mix Drops' seals in the freshness—protects heat and moisture-labile vitamins (especially B_{12}) by keeping them in stable, powder-dry form until ready for use. Until mixed, no refrigeration is required. Pharmacist or parent adds the separately packaged vehicle to the bottle containing the powder. The resultant solution is sparkling clear, fully potent.

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Lilly

Prescribe either the 30-cc. or 60-cc. package.

'Vi-Mix Drops'

(MULTIPLE VITAMIN DROPS, LILLY)

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for
March 15
1953

Modern Medicine
Vol. 21, No. 6

●

THE MAN ON THE COVER is Dr. Reed M. Nesbit of Ann Arbor, Professor of Surgery at the University of Michigan Medical School and Chief of the Section of Urology at the University Hospital. Dr. Nesbit is a member of the American Association of Genito-Urinary Surgeons, American Urological Association, and International Society of Urology. Editor of *American Lectures in Urology*, Dr. Nesbit is author of *Fundamentals of Urology*, *Transurethral Prostatectomy*, and *Prostatectomia Transuretra*. The report on page 116, "Hydronephrosis in General Practice," is based on an original article by Dr. Nesbit which appeared in the *Nebraska Medical Journal*.

Contents for March 15 1953

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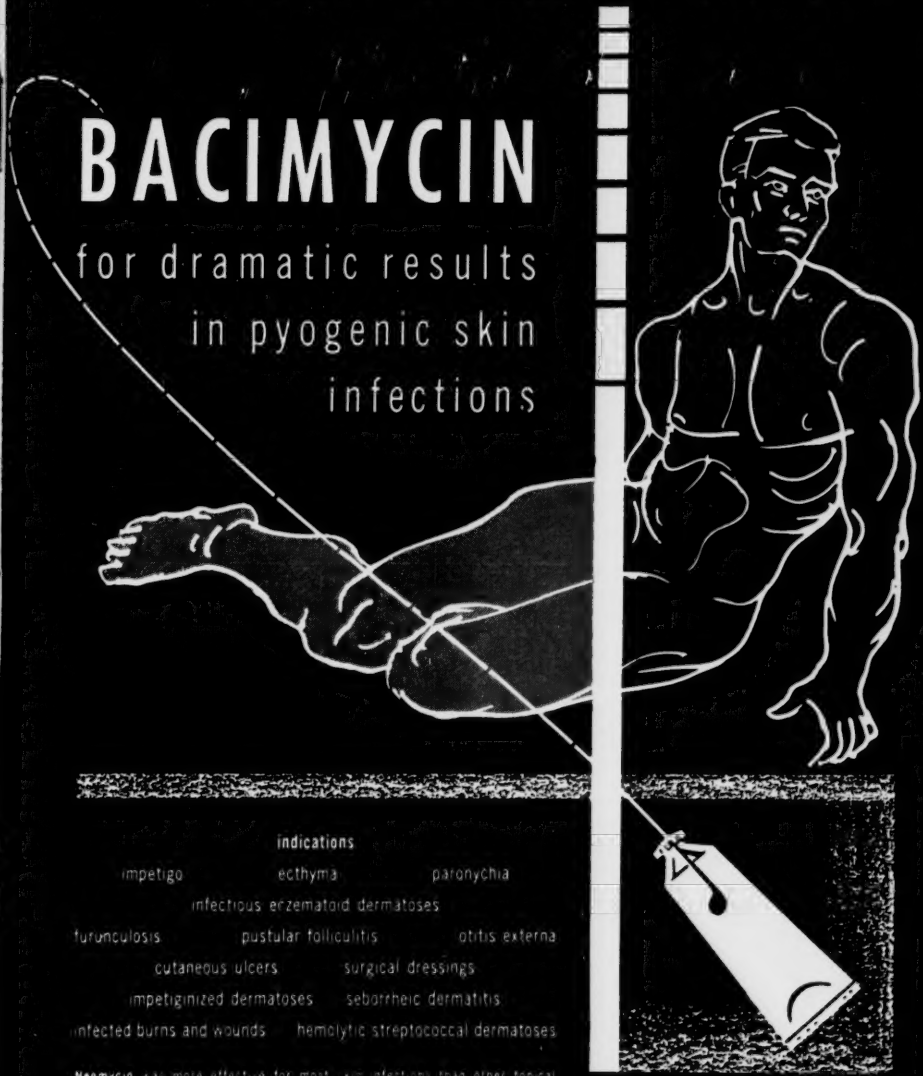
BACITRACIN NEOMYCIN OINTMENT

BACIMYCIN

for dramatic results in pyogenic skin infections



indications

impetigo ecthyma paronychia
infectious eczematoid dermatoses
furunculosis pustular folliculitis otitis externa
cutaneous ulcers surgical dressings
impetiginized dermatoses seborrheic dermatitis
infected burns and wounds hemolytic streptococcal dermatoses

Neomycin was more effective for most skin infections than other topical agents used in a series of 675 cases.[1]

Bacitracin has been widely favored for local treatment of skin infections.[2]

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LETTER FROM THE EDITOR

Dear Reader:

From time to time it is good to recapitulate our knowledge, especially in those areas in which developments have been rapid. The field of the autonomic drugs has been one of considerable activity recently and much progress has been made in the use of these agents in the treatment of disease.

Dr. John C. Krantz, Jr., Professor of Pharmacology at the University of Maryland and a member of the National Editorial Board of *Modern Medicine,* has arranged for a series of special articles summarizing progress in the therapeutic application of agents acting on the autonomic nervous system. These articles are presented as a Symposium beginning on page 127 of this issue.

Another feature of particular note will be found on pages 102-113. It is a special exhibit adapted from the splendid presentation of Dr. Charles A. Janeway and H. D. Piersma made at the clinical session of the American Medical Association in Denver last winter. By means of attractive charts and tables, the exhibit tells what gamma globulin consists of, how it is derived, the various antibodies that have been found in gamma globulin, and how gamma globulin has been applied to clinical medicine.

The editors are very pleased to be able to include these distinguished contributions to the understanding of two important subjects in this issue. These are truly bonus features offered to our readers in addition to the comprehensive coverage of the current literature of medicine. We are sure you will find much of value and interest in them.

Walter C. Alvarez

EDITOR-IN-CHIEF

IN GERIATRICS...

"Subclinical Hypothyroidism" may be the answer

One of the subtle changes of advancing age, which may result in myocardial damage, anemia and intellectual retrogression, is mild hypothyroidism which "is far more prevalent than is generally realized."[1]

In the group studied, Kimble and Stieglitz found chronic fatigue the most prominent symptom, with diminished cold tolerance, tendency to gain weight, generalized muscular aches, poor memory, palpitation and constipation frequent complaints.

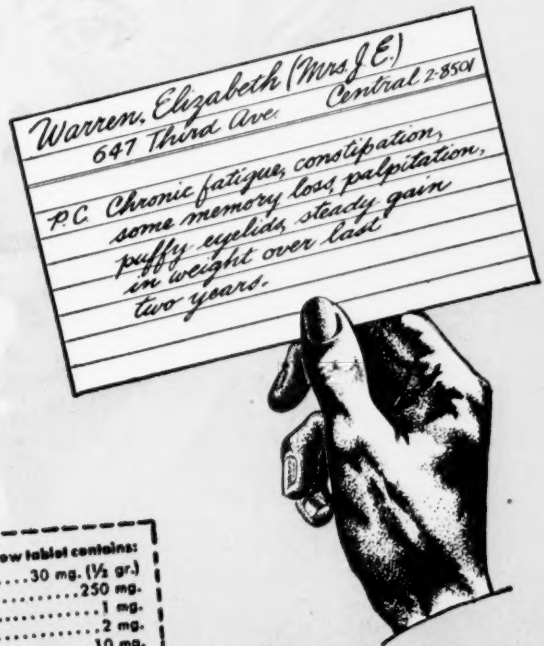
Thyrobex*

Thyrobex contains thyroid Duo-sayed—check-tested by two assays** and B vitamins—as increase of the metabolic rate demands increased vitamin B complex intake. In addition Thyrobex supplies the antithyrotoxic factor of liver which has been shown to offset side reactions to thyroid.

*Trademark

**Thyrobex contains Thyroid Duo-sayed®—assayed for total iodine content and thyroxin content, for more reliable results.[2]

1. Kimble, S. T., and Stieglitz, E. J.: Hypothyroidism: A Geriatric Problem, Geriatrics 7:20-31 (Jan.-Feb.) 1952.
2. Robertson, J. D., and Kirkpatrick, H. F. W.: Brit. M. J. 1:624 (Mar. 22) 1952.



Each capsule-shaped, yellow tablet contains:

Thyroid Duo-sayed®	30 mg. (½ gr.)
Liver Desiccated, N.F.	250 mg.
Thiamine Hydrochloride	1 mg.
Riboflavin	2 mg.
Niacinamide	10 mg.
Vitamin B_{12}	1 mcg.

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Correspondence

Communications from the readers of MODERN MEDICINE *are always welcome. Address communications to The Editors of* MODERN MEDICINE, *84 South 10th St., Minneapolis 3, Minn.*

Weeping Otitis Externa

TO THE EDITORS: Now that reasonably effective therapeutic measures are available in the management of otitis externa in which *Pseudomonas aeruginosa* is isolated, situations such as the one submitted to your Questions & Answers department (*Modern Medicine*, Jan. 1, 1953, p. 32) are being encountered ever more frequently.

We have found too that neomycin works fairly effectively in this condition, but I would like to enter one factor which we feel is of primary importance in therapy. When the lesion is "dry and scaly," neomycin ointment is the agent of choice; however, in weeping stages due to scratching, picking, sensitivity response to fingernail lacquer on the picking finger, or overtreatment, we find that Burow's solution used alternately with neomycin (topical 0.5-gm. lyophilized tablet added to 100 cc. distilled water) provides the drug in a menstruum not occlusive for the weeping stage. With eczematization of the "dry stage," the ointment is of greatest value as recommended by your consultant.

CLIFFORD H. KALB, M.D.
Milwaukee

Trauma Issue Valuable

TO THE EDITORS: Will you please send me the number of *Modern Medicine* which contained your "Symposium on Trauma." This was a very valuable number. My copy has been misplaced, so I would like very much to have another one if possible.

R. H. BASKIN, M.D.

¶ A limited number of copies of the "Symposium on Trauma" are still available and will be sent on request until the supply is exhausted.—Ed.

Chronic Brucellosis

TO THE EDITORS: The diagnostic problem in chronic, low-grade, relatively afebrile brucellosis is involved. Many patients have neurotic symptoms, related or unrelated, which add to the difficulty in diagnosis. Since these patients are usually not ill enough to be confined to the hospital, the best opportunity to study them adequately is in private practice.

There is no uniform clinical picture. Detection depends more on inclusion of brucellosis in differential diagnostic thinking and on the use of a manifold battery of labora-

(Continued on page 26)

CONSTIPATION*

possibly the

greatest single medical problem

of the patient who is over **40**

In these cases, laxation *alone* isn't enough.

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*Rehfuss, M. E.: Indigestion, Philadelphia, W. B. Saunders Co., 1943, p. 322

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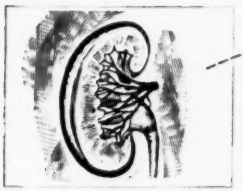
(phentolamine methanesulfonate Ciba), preferred in the diagnosis of pheochromocytoma, the cause of the most common form of hypertension of *known* etiology. The injection of this *adrenergic blocking agent* affords an accurate test that is relatively safe, and can be simply performed by any physician, unassisted, in his office.



three new agents in the control of hypertension

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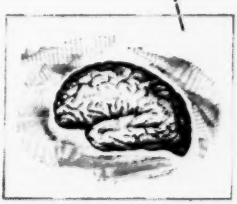
Esomid®

chloride (hexamethonium chloride Ciba), a potent oral hypotensive agent, may be particularly valuable in those patients with severe hypertension which has failed to respond to Apresoline. Esomid acts as a *ganglionic blocker*, inhibiting the transmission of impulses through all autonomic ganglia.



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hydrochloride (hydralazine hydrochloride Ciba), an agent of choice (for use) in the treatment of hypertension. This orally effective antihypertensive is believed to act *centrally* to produce a gradual, sustained decrease in blood pressure while increasing blood flow through the kidneys.

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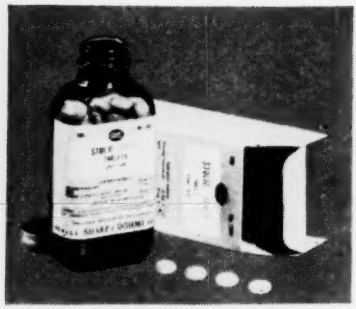
STOLIC FORTE Tablets serve a double purpose for more efficient management of essential hypertension. Prolonged vasodilation and mild sedation are attained simultaneously with STOLIC FORTE Tablets, thus eliminating the necessity for administering two medicaments.

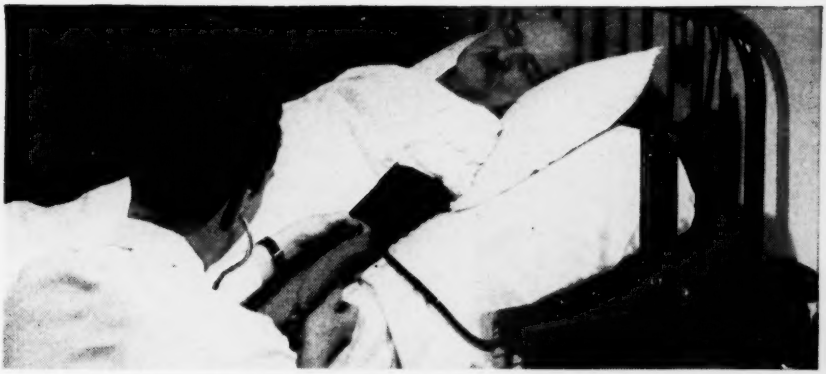
SHARP & DOHME

It is well known that retinal hemorrhages and progressive disturbances in the retinal vascular bed are manifestations of hypertension.



STOLIC FORTE *Tablets are supplied in bottles of 100 and 1,000. A modification of the* STOLIC FORTE *formula, containing one-half the amount of mannitol hexanitrate (15 mg.) is available as* STOLIC.

in hypertension



STOLIC FORTE *Tablets may be relied upon to reduce systolic and diastolic pressure in hypertension, and relieve concomitant symptoms, such as dizziness, headache, dyspnea, palpitation, nervousness and apprehension.*

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TABLETS

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The STOLIC FORTE formula also contains 30 mg. DELVINAL® per tablet to allay apprehension and level off fluctuations in blood pressure due to emotional tension. DELVINAL is characterized clinically by its moderate duration of action and the fact that the patient experiences little of the so-called "drugged sensation" or other undesirable side-effects with its use.

Sharp & Dohme, Philadelphia 1, Pa.

1. Krantz, J.C., Jr., & Carr, C.J.: The Pharmacologic Principles of Medical Practice, The Williams & Wilkins Co., Baltimore, Md., 1951, p. 836.

tory tests than it does on diagnostic acumen. In addition to fatigue, which is common to so many somatic and psychogenic illnesses, there is scarcely a known complaint which may not be voiced by patients with culturally proved brucellosis. Evidence of psychoneurosis does not rule out concurrent or perhaps causally related brucellosis.

Diagnostic criteria for acute febrile brucellosis or febrile exacerbations of chronic brucellosis seldom are applicable to the chronic illness when there is little or no fever. In these cases, which outnumber the febrile cases by a ratio of about 10:1, agglutinins are likely to be present only in low titer, if at all. Bacteremia is rarely present but culture of tissue removed at operation or biopsy may show the organism. Therefore culture and agglutination reaction, so helpful in the diagnosis of the acute illness, cannot be relied upon to detect the chronic cases. Occasional proof of the correctness of this theory is furnished by positive cultural findings in the absence of agglutinins or any other significant laboratory findings.

A practical diagnostic approach to the problem of chronic brucellosis has developed gradually since 1932, incorporating and modifying methods and ideas contributed by various authorities—Foshay, Simpson, Huddleson, Castaneda, and others—as follows:

History of present and past illness includes questioning as to ingestion of unpasteurized dairy products or contact with the organism in cattle, goats, hogs, or horses or in laboratory work. Frequently,

(Continued on page 30)

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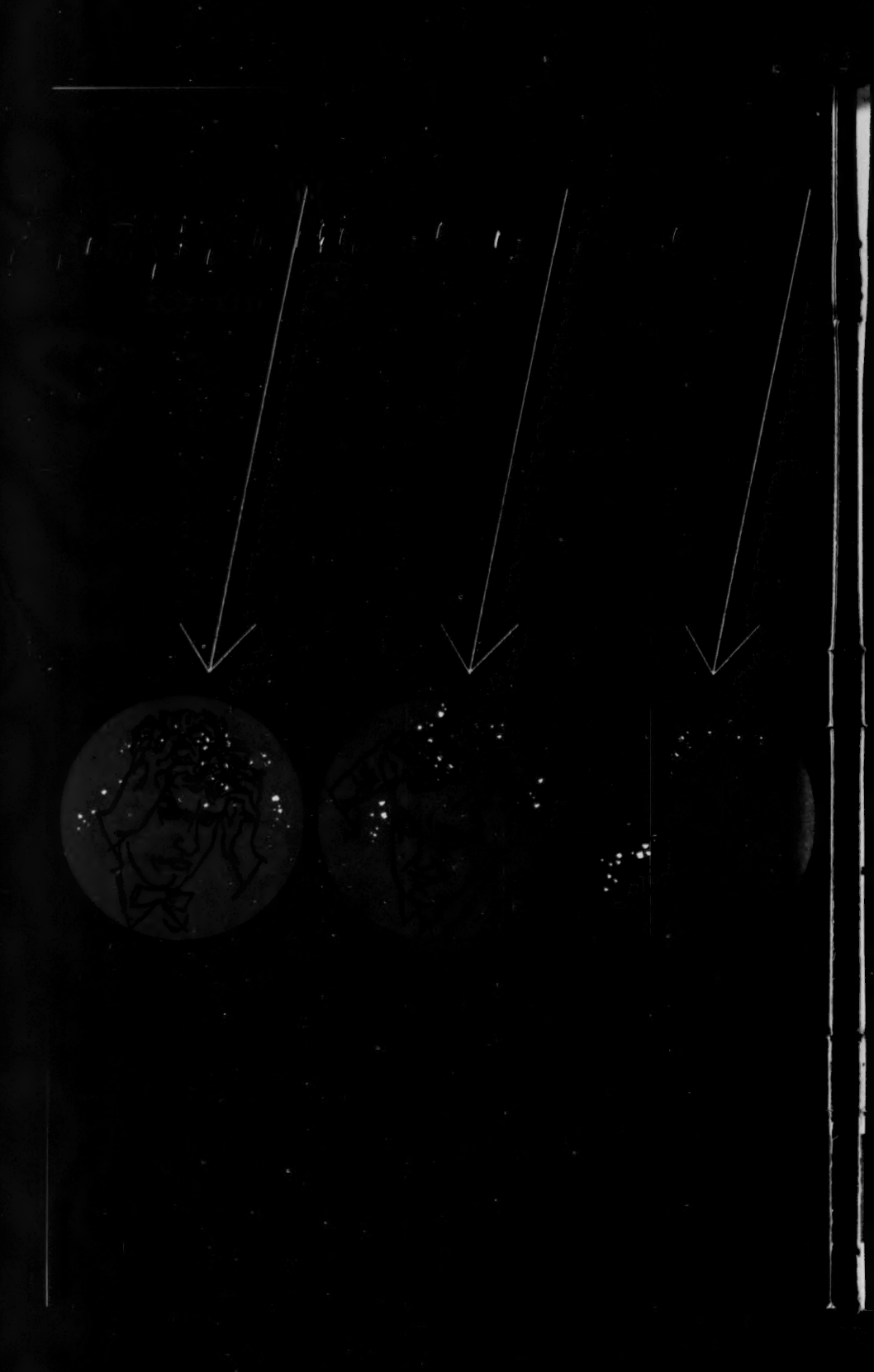


who have Seborrheic Dermatitis of the scalp . . . prescribe

this effective new product

Effective control of scaling . . . prompt relief of itching and burning . . . extreme simplicity of use . . . this is the story of SELSUN Sulfide Suspension, Abbott's new *prescription-only* product for the management of seborrheic dermatitis of the scalp. Clinical investigators who treated 400 patients[1, 2, 3] found SELSUN effective in 92 to 95 percent of cases of mild seborrhea (common dandruff), and in 81 to 87 percent of all cases of seborrheic dermatitis.

SELSUN was successful in many cases that had failed to respond to other recognized methods of treatment. Optimum results were obtained in four to eight weeks, although itching and burning stopped after the second or third application in most cases. After the initial treatment period, a single application keeps the scalp free of scales for one to four weeks.

SELSUN is convenient to use, because it is simply applied while washing the hair and then rinsed out. It thus leaves the hair clean and odorless, and obviates the problem of stains on clothing and linens. Specific research on toxicity[1, 2] shows there are no harmful effects from external use of SELSUN as recommended. Supplied by pharmacies in 4-fluidounce bottles, with tear-off labels. Dispensed only on a physician's prescription. Abbott

References:

1. Slinger, W. N., and Hubbard, D. M. (1951), Arch. Dermat. & Syph., 64:41, July.
2. Slepyan, A. H. (1952), Ibid., 65:228, February.
3. Ruch, D. M. (1951), Communication to Abbott Laboratories.

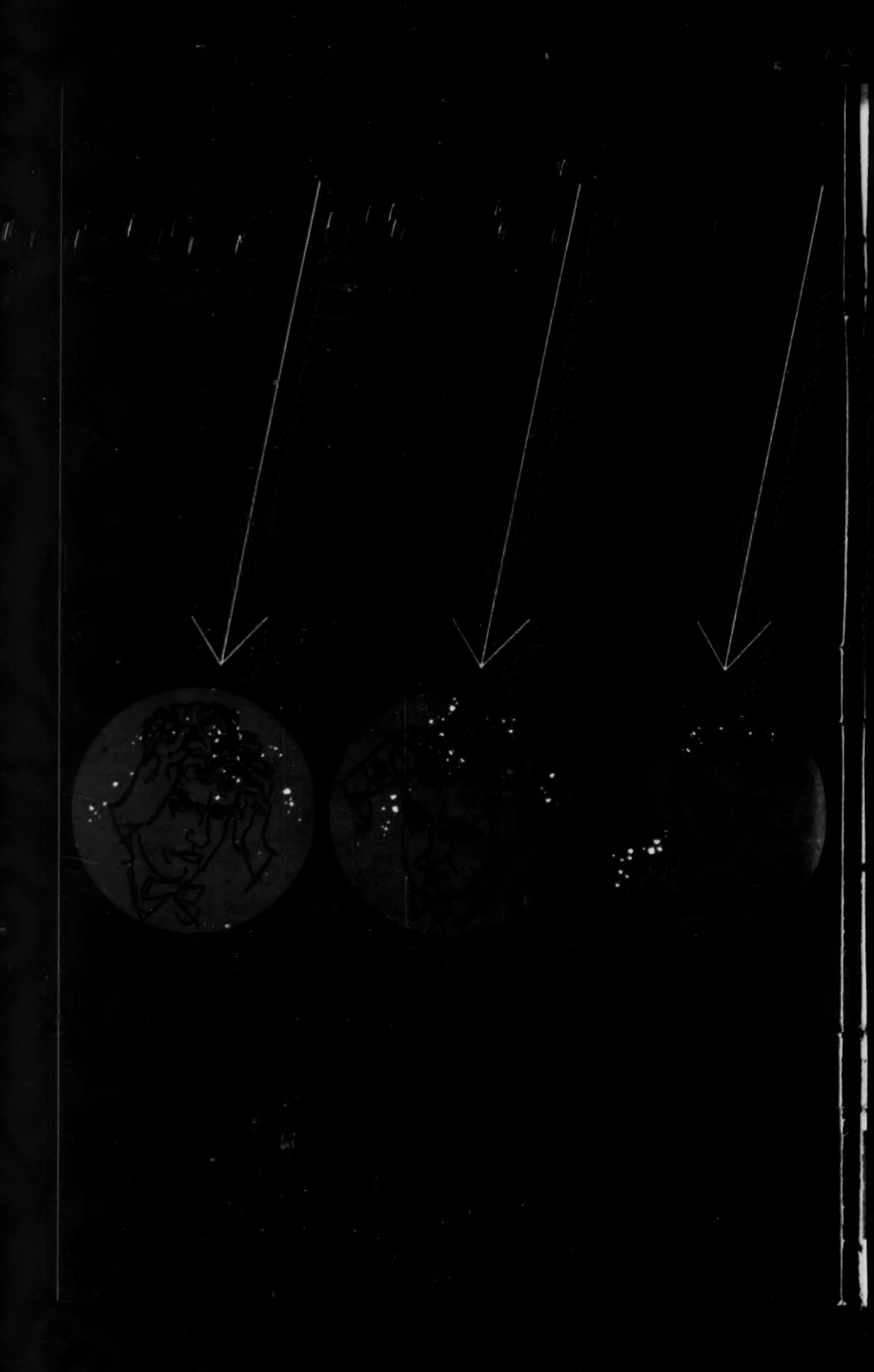
PRESCRIBE **SELSUN**

TRADE MARK

SULFIDE *Suspension*

(SELENIUM SULFIDE, ABBOTT)

D



who have Seborrheic Dermatitis of the scalp . . . prescribe

this effective new product

Effective control of scaling . . . prompt relief of itching and burning . . . extreme simplicity of use . . . this is the story of SELSUN Sulfide Suspension, Abbott's new *prescription-only* product for the management of seborrheic dermatitis of the scalp. Clinical investigators who treated 400 patients[1, 2, 3] found SELSUN effective in 92 to 95 percent of cases of mild seborrhea (common dandruff), and in 81 to 87 percent of all cases of seborrheic dermatitis.

SELSUN was successful in many cases that had failed to respond to other recognized methods of treatment. Optimum results were obtained in four to eight weeks, although itching and burning stopped after the second or third application in most cases. After the initial treatment period, a single application keeps the scalp free of scales for one to four weeks.

SELSUN is convenient to use, because it is simply applied while washing the hair and then rinsed out. It thus leaves the hair clean and odorless, and obviates the problem of stains on clothing and linens. Specific research on toxicity[1, 2] shows there are no harmful effects from external use of SELSUN as recommended. Supplied by pharmacies in 4-fluidounce bottles, with tear-off labels. Dispensed only on a physician's prescription. Abbott

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PRESCRIBE **SELSUN**

TRADE MARK

SULFIDE *Suspension*

(SELENIUM SULFIDE, ABBOTT)

D

patients state that no milk is used but that they do use cream; many wrongly consider certified milk entirely safe even though raw. Negative histories of known recent exposure are unreliable since the infection may be of many years' duration.

Because of the many neurotic manifestations so often encountered in the chronic illness, the usual history is supplemented by a psychiatric history and examination. In all obscure problems a battery of projective psychologic studies, including the Rorschach method, figure drawing, sentence completion, and thematic apperception, is carried out by an expert clinical psychologist.

Although physical findings in chronic brucellosis are usually few, splenitis, hepatitis, cirrhosis, cholecystitis, mixed types of arthritis, true neuritis, and low-grade chronic meningitis are among the many possible findings.

Laboratory studies include complete blood count, sedimentation rate, urinalysis, blood chemistry, Wassermann, chest roentgenogram, and specific tests for brucellosis—blood agglutination, complement fixation, opsonocytophagic and intradermal reactions, and blood culture using the special technics essential for the isolation of *Brucella*. In addition, special procedures of differential diagnostic value are used as indicated.

The data are correlated in the following manner:

- Negative agglutination reactions do not rule out brucellosis. Blood or tissue cultures may be positive in the absence of agglutinins.
- Agglutination reactions in low titer, below 1:80, are looked upon

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And MAXISERVICE also means

1. NO INITIAL INVESTMENT

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With MAXISERVICE, you never have an investment in obsolete equipment. When your apparatus is outmoded by new developments, General Electric will replace it with the new design — you never suffer obsolescence loss!

You get all these MAXISERVICE advantages at a cost that's *actually less than if you bought the x-ray apparatus outright!* Ask your GE x-ray representative to show you comparative figures, or write X-Ray Department, General Electric Company, Milwaukee 1, Wisconsin, for Pub. G-3.

1876 75 1951 YEARS OF ELECTRICAL PROGRESS

GENERAL ELECTRIC

as probable indications of active or inactive infection. The possibility of cross-agglutination due to infection without organisms is investigated. Previous prophylactic use of cholera vaccine or *Brucella* antigens is considered.

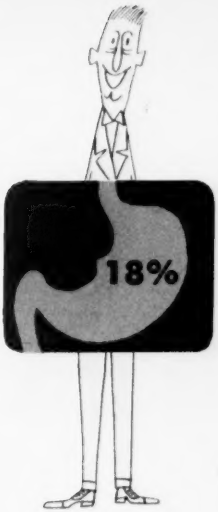
• Agglutination tests are repeated since rising titers may be found in the presence of acute or subacute exacerbation.

• The opsonocytophagic reaction of moderate to high degree points to past or current infection but does not distinguish between them. A low, so-called "negative" reaction may only indicate lack of immune response.

• The blood complement-fixation reaction usually parallels the agglutination reaction but may be positive earlier or when agglutinins are persistently absent.

• Blood culture for *Brucella* or other pathogens is carried out whenever there is even low-grade fever because of the rare chance that the organism may be in the blood. Spinal fluid, synovial fluid, bile, urine, feces, and discharges are cultured whenever *Brucella* is indicated.

• The intradermal test is reserved until blood studies are completed because of the probable stimulation of agglutinins, opsonins, and complement. It is performed with an antigen of known reliability such as killed *Br. abortus* organisms. Varying dilutions are used in the



Compare recurrence rates on ulcer therapies old and new

Standard therapy, 42%

The critical problem of ulcer recurrence is illuminated by reports on 13,537 ulcer patients during fifty years. A summary of 64 reports showed 42 per cent recurrence on standard therapy.[1]

Mucin-antacid, 18%

Recurrences totaled *only 18 per cent* when Hardt and Steigmann treated 125 ulcer patients with mucin-antacid mixture and followed them for two years.[2]

TRIMUCOLAN®

A NEW MUCIN-ANTACID FOR LOWER RECURRENCE RATES

The Council on Pharmacy and Chemistry of the American Medical Association states:[3] "Gastric mucin imparts to the mixture a more distinct protective coating effect on the gastric mucosa than can be demonstrated with the use of antacids alone . . ."

". . . best results are obtained with preparations containing approximately 10 per cent of gastric mucin. A ratio of 1:1.5:2.75 for gastric mucin—aluminum hydroxide—magnesium trisilicate produces good results."

These "best results" now with TRIMUCOLAN: mucin + reactive aluminum hydroxide + magnesium trisilicate.

WINTHROP

1. Bralow, S. P., Spellberg, M., Kroll, H., and Neches, H.: Am. Jour. Digest. Dis., 17:119, Apr. 1950.
2. Hardt, L. L., and Steigmann, Frederick: Am. Jour. Digest. Dis., 17:195, June, 1950.
3. New and Nonofficial Remedies, Council on Pharmacy and Chemistry, American Medical Association, Philadelphia, J. B. Lippincott Co., 1952, p. 312.

***Important offer* — see reverse side. ▶**

To change the ulcer recurrence picture

a new mucin-antacid

TRIMUCOLAN

On the reverse side of this page you will see figures on a possible decline from 42 per cent to 18 per cent in ulcer recurrence. *Investigators used mucin-antacid* for the good results.

Why you can expect fewer recurrences with TRIMUCOLAN

1. Relieves pain almost as promptly as soluble alkalis but without rebound or alkalosis.
2. Coats and clings to ulcer and entire gastric mucosa uniformly.
3. Remains in stomach *longer* — exerts prolonged antacid action.
4. Retards pepsin activity and inhibits mucosal erosion.
5. Reduces the likelihood of ulcer recurrence by at least 50 per cent.

Send now for helpful supply.

TO: *Winthrop Stearns* Inc., 1450 Broadway, New York 18, N. Y.

Please send samples of Trimucolan,® a new mucin-antacid to help keep down ulcer recurrence rate.

NAME.....M.D.

STREET.....

CITY.....ZONE.....STATE.....

Turn the page — read about important ulcer studies.

780M

presence of suspected *Brucella* infection or allergy involving the central nervous system or the eye because of possibly severe and irreversible allergic focal reaction. Brucellergen is not used because it is a relatively insensitive antigen, giving approximately 50% fewer positive reactions than killed whole *Brucella* organisms.

• A positive skin test is interpreted to indicate that the patient has been rendered allergic to *Brucella* through infection, although perhaps subclinical or symptomless, comparable in significance to the tuberculin reaction. Patients with moderate reactions frequently report improvement in all previous or current symptoms within a few days following the test. Hypersensitive patients with violent reactions usually report marked intensification of symptoms for a few days during the height of the skin reaction, often then followed by moderate to complete remission of symptoms for periods of weeks or even years. This mechanism is based on desensitization and immunization and is reflected in a commensurate rise in the phagocytic power of the white cells against *Brucella* in most instances. There also may be objective evidence of this incidental effect of the skin testing dose of *Brucella* antigen, such as prompt subsidence of swelling and tenderness of a joint or disappearance of

(Continued on page 242)

in ARTHRITIS *and allied disorders*

BUTAZOLIDIN

rehabilitates the disabled patient

Through the use of BUTAZOLIDIN, many patients formerly bedridden, are now able to resume an active and useful life.

A totally new, synthetic compound, BUTAZOLIDIN (brand of phenylbutazone) is not related to the steroid hormones and its therapeutic effects are not dependent upon alteration of hormonal balance.

Clinically, BUTAZOLIDIN affords relief of pain, ranging from mild to complete, in approximately 75 per cent of cases. In the majority of instances, BUTAZOLIDIN also produces increased ease and range of motion through diminution of swelling and spasticity.

Characteristically effective in almost all forms of arthritis as well as in other painful musculoskeletal disorders, BUTAZOLIDIN affords the convenience of oral administration and the economy of relatively low cost.

Rheumatoid Arthritis[1-6]
Osteoarthritis[1,3,5]
Ankylosing Spondylitis[1,3-5]
Gout[1,4,5]
Psoriatic Arthritis[1,3,5]
Peritendinitis of the Shoulder[1,2,3,5]
Mixed Arthritis[1,5]
Bursitis[2]
Capsulitis[2]
Calcific Tendinitis[3]
Reflex dystrophy[3]
Menopausal arthralgia[3]
Lumbosacral strain[3]
Malum coxae senilis[5]
Still's disease[5]

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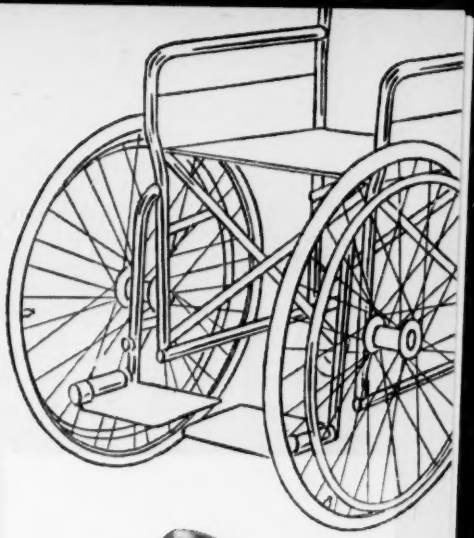


BUTAZOLIDIN has been reported to produce favorable results in all of the listed indications.

Treatment of the more transient conditions may be discontinued a few days after symptoms have been completely relieved. In the more chronic disorders BUTAZOLIDIN is usually continued indefinitely at the minimal effective dosage level required to avoid relapse. Frequently, the initial dosage of 600-800 mg. daily may be reduced to 400 mg. daily, or even less, without loss of effect.

In order to secure optimal results with minimal risk of side reactions physicians are urged to send for the brochure, "Essential Clinical Data on BUTAZOLIDIN," and other informative literature.

BUTAZOLIDIN® (brand of phenylbutazone) is available as coated tablets of 200 mg. and 100 mg.

Questions & Answers

All questions received will be answered by letter directed to the petitioner; questions chosen for publication will appear with the physician's name deleted. Address all inquiries to the Editorial Department, MODERN MEDICINE, *84 South Tenth Street, Minneapolis 3, Minnesota.*

QUESTION: What is the relative percentage of recovery for patients with herniated intervertebral disk treated by conservative methods, such as braces, exercises, and sedatives, compared with results obtained by surgery?

M.D., Massachusetts

ANSWER: *By Consultant in Orthopedics.* Equally good results are claimed for both conservative and surgical management of ruptured disks. Most doctors now believe in a reasonable trial of conservative treatment before intervention by surgery. Surgery is indicated in recurrent cases.

QUESTION: A 45-year-old woman has had attacks of erosion of the tongue for ten years, sometimes of the buccal surfaces. These areas are not deep but are painful, serpentine markings, often white or scarlet with white borders and travel over the mucous membrane leaving a normal surface behind. The condition rarely clears and often becomes severe. She has had allergy tests, many kinds of vitamin treatments, topical applications, and so forth, with no benefit. All serologic reactions are normal. What is this condition and what is the treatment?

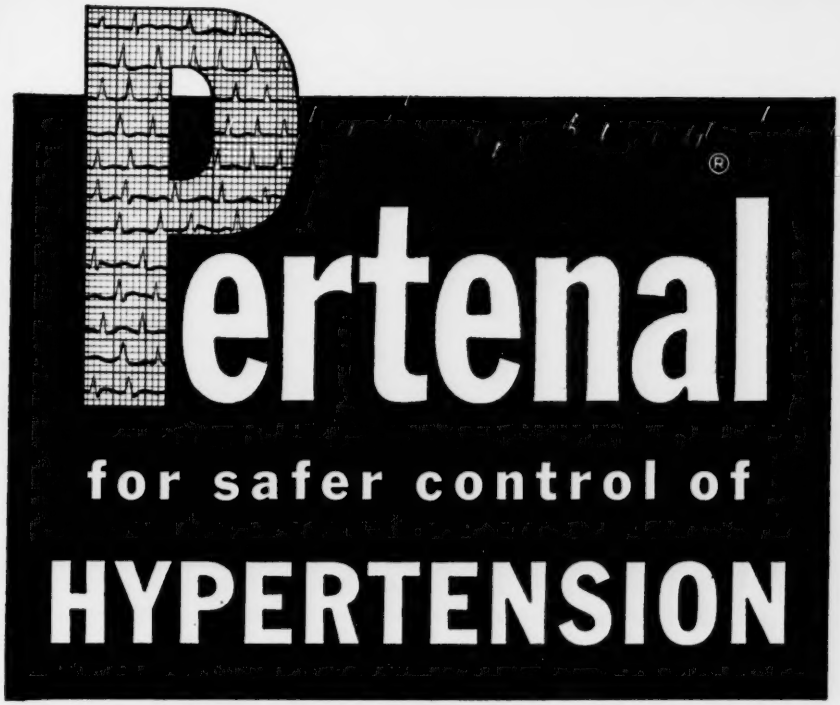
M.D., Montana

ANSWER: *By Consultant in Dermatology.* The condition described probably is an example of transitory benign plaques of the tongue, sometimes known as geographic tongue. Little is known of their cause and no satisfactory treatment is recognized. During an attack, the patient should avoid foods which have made her more uncomfortable in the past. Frequently, tomatoes, berries, and nuts should be avoided, especially walnuts. Except for use of a mild mouthwash or irrigation, no benefit is obtained from local therapy.

QUESTION: What treatment do you advise for a patient with onychomycosis of the nails caused by *Trichophyton purpureum?*

M. D., New York

ANSWER: *By Consultant in Dermatology.* Onychomycosis is difficult to cure, particularly when caused by *Trichophyton purpureum.* Sometimes this disease responds to surgical avulsion of the infected nail followed by soothing treatment of the wound for about the first ten days and then by fungicidal therapy such as a diluted Whitfield's ointment, the concentration of which can be increased gradually according to tolerance. During this time every possible attempt should be made to clear up any other foci of dermatomycosis which may be present.



In PERTENAL the potent vasodilator, mannitol hexanitrate, supplements the hypotensive action of veratrum, allowing the veratrum to take effect at a lower blood pressure level . . . assuring well sustained reduction of pressure, with minimal, *safer* veratrum dosage, *and* prompt relief of headache, dizziness, worry, restlessness, insomnia, gastrointestinal discomforts and other symptoms which often aggravate pressure.

PERTENAL treats the patient as a whole — helps assure
a more comfortable, more tranquil, often longer life.

Dose: 1 tablet every 4 to 6 hours.

Supplied in bottles of 50, 100 and 500 tablets.

each PERTENAL tablet contains:

Veratrum Viride (standardized extract of the whole drug)	100 mg. (1½ gr.)
Homatropine Methylbromide	2.5 mg. (1/25 gr.)
Mannitol Hexanitrate	30 mg. (½ gr.)
Phenobarbital	15 mg. (¼ gr.)

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CROOKES LABORATORIES, INC. Crookes MINEOLA, NEW YORK

Therapeutic Preparations for the Medical Profession

When you think of oral penicillin

Dram

the most complete line of liquid oral penicillin

Whatever the indication or the patient's age, you will find a palatable Dramcillin product exactly suited to your needs. *White's* Dramcillin "family" assures:

wide therapeutic control

greater convenience

fewer hypersensitivity reactions

ready patient-acceptance

specify *White's*

cillin

and penicillin-sulfonamide preparations

Dramcillin-500 (500,000 units* per teaspoonful)

Now available in both 30 cc and 60 cc bottles, supplying 6 and 12 teaspoonfuls respectively.

Dramcillin-250 (250,000 units* per teaspoonful)

Dramcillin-500 and Dramcillin-250 place oral penicillin therapy on convenient t.i.d. or b.i.d. basis.

Dramcillin-250 with Triple Sulfonamides

(250,000 units penicillin* and 0.5 Gm. sulfas† per teaspoonful)

Dramcillin-250 Tablets with Triple Sulfonamides

(250,000 units penicillin* and 0.5 Gm. sulfas† per tablet)

Dramcillin with Triple Sulfonamides

(100,000 units penicillin* and 0.5 Gm. sulfas† per teaspoonful)

Dramcillin (100,000 units* per teaspoonful)

Dropcillin (50,000 units per dropperful—0.75 cc.)

**Crystalline penicillin G potassium*

†*0.167 Gm. each of sulfadiazine, sulfamerazine and sulfacetamide*

White Laboratories, Inc., Kenilworth, N. J.

QUESTION: What is the average dosage of pyridoxine (B_6)? Has it proved beneficial in psychologic nervous diseases?

M. D., Illinois

ANSWER: *By Consultant in Neurology.* Pyridoxine (B_6) is given intravenously in doses of 100 mg. daily or every other day for two or three weeks. The vitamin has not proved to be of benefit in the treatment of psychologic nervous diseases.

QUESTION: A tall, slender, 60-year-old schoolteacher had a partial gastric resection in 1941 and a second in 1951. The first was for an ulcer and the second for a marginal ulcer. Since the latter operation, she has experienced considerable diarrhea, especially if she takes milk. Microscopic blood was found in the stools and the hemoglobin has dropped since the last operation to between 9 and 10 gm. At present she weighs 100 lb., but eats well. No question of malignancy has ever arisen. She has been investigated for potassium, vitamin K, and B_{12} deficiency. All attempts to find a suitable diet have failed, including treatment by an allergist. Can you suggest some means by which this patient can gain weight?

M.D., California

ANSWER: *By Consultant in Gastroenterology.* When a large part of the stomach has been removed, multiple nutritional and vitamin deficiencies may occur. The diarrhea may be from fat intolerance or lack of free hydrochloric acid. The anemia may be from blood loss, possibly from gastritis or jejunitis, and iron deficiency. Requirements then would be a high-calorie, high-protein, low-fat diet with iron and folic acid. Calcium may be needed and vitamin B complex, perhaps by injection. If diarrhea persists, diluted hydrochloric acid may be given with meals.

PEDIATRICS BULLETIN

Prepared In The Interests Of The Profession By The Pediatrics Consultant Staff Of H. J. Heinz Company

Immunization procedures and **POLIOMYELITIS**

CONSIDERABLE concern has arisen regarding the importance of a relationship between routine immunization procedures and the incidence or localization of paralysis from poliomyelitis. Results of a conference to consider this were summarized in the J.A.M.A.* last year. It was concluded that there was evidence of such association, though it was probably not quantitatively great.

● **Due to the highly** emotional reaction of the public in its fear of poliomyelitis, inevitable public knowledge of this situation could interfere with well-established and invaluable immunization programs. It is, however, quite possible to devise an immunization program which aids in avoiding even a theoretical risk. The factors which permit such a program are: (1) Fairly solid immunity to poliomyelitis persists until after six months of age. (2) Immunization programs might advantageously be started at the age of three months. (3) The timing of booster shots is surely elective and they can be given out of epidemic season.

● **Until more** certainty exists about this matter, the public must be reassured that by adopting some such program, no risk is taken that can be avoided without incurring still greater risks.

NOTE: These bulletins are designed to help disseminate modern pediatrics knowledge to the general medical profession and will appear monthly in Modern Medicine.

Journal of the American Medical Association, Vol. 149, p. 170, May 10, 1952

Forensic Medicine

ARTHUR L. H. STREET, LL.B.

Prepared especially for Modern Medicine

PROBLEM: In a workmen's compensation proceeding, there was no denial that hospital and medical treatment had been reasonably given to the employee claimant. In the absence of contrary evidence, was the testimony of a hospital manager and a doctor as to the reasonableness of the charges conclusive, neither witness being pecuniarily interested in the particular allowances?

COURT'S ANSWER: Yes.

So decided the Texas Civil Court of Appeals, Waco (252 S. W. 2d 589).

PROBLEM: A 1952 New York law authorizes the state commissioner of health to requisition for scientific tests and experimental use, in lieu of destruction, unlicensed, unwanted, or unclaimed animals seized and impounded by municipalities or authorized private organizations. Were owners of cats and dogs not seized entitled to challenge the constitutionality of the law in court?

COURT'S ANSWER: No.

The New York Supreme Court, Westchester County, strongly intimated that the law is constitutional, but found it unnecessary to decide that point. The court applied the general rule that one is not entitled to challenge the constitutionality of a law unless his rights have been, or are about to be, infringed.

A humane society was declared to be without standing to complain of the new law because there was no more than a remote possibility that animals in its custody would be seized.

The court did recognize that owners of cats and dogs have property rights in them, subject to reasonable police regulations (116 N. Y. Supp. 2d 403).

PROBLEM: In a football coach's suit for damages after his employment had been terminated, the vital question was whether he was physically incapable of performing his duties. Without objection by the coach's attorney, defendant called as a witness Dr. P, who had examined the coach as a patient. Dr. P testified that he had familiarized himself with hospital records, including a diagnosis of coronary thrombosis by Dr. F. Defendant then called Dr. F. Was the coach entitled to have Dr. F's testimony excluded on the ground that Dr. F was disqualified to testify adversely to his patient?

COURT'S ANSWER: No.

The New York Supreme Court, Appellate Division, First Department, reasoned: When Dr. P was permitted to testify, although the trial judge informed plaintiff that he would thereby waive right to object, that not only waived Dr. P's disqualification to testify but also waived objection to testimony of any other doctor who had examined plaintiff as to the particular ailment involved (116 N. Y. Supp. 2d 318).

In the menopause

COMPLAINTS RELATED TO
DISTURBED AUTONOMIC
PHYSIOLOGY.....

Psychic fears... **MALIGNANT DISEASE**
NERVOUS BREAKDOWN
LOSS OF CHILDREN
LOSS OF PHYSICAL AND SEXUAL ATTRACTION

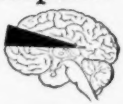
BELLERGAL®

for smooth transition in the Menopause

...Somatic complaints **DYSPAREUNIA**
MENORRHAGIA
ENDOMETRIAL HYPERPLASIA
HOT FLUSHES
PALPITATION
DYSPNEA
VERTIGO

Autonomic Instability Related to Menopausal Symptoms

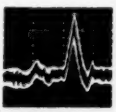
Kroeger and Freed[1] state that there are three main categories of the psychiatric manifestations of the menopause: (1) emotional disturbances which arise at this time of life without any significant history of similar episodes in the preceding years, (2) exacerbation of previous neurotic tendencies, and (3) psychoses of various types which appear at this time or often a few years later, with one large group outstanding, such as involutional melancholia.



NERVOUS AND PSYCHIC COMPLAINTS

"All of these conditions and experiences involve the autonomic nervous system and affect the psyche as well as the soma."[2]

Harris[3] is of the impression that disturbing somatic symptoms are autonomic in origin. "The majority of complaints of the menopause are connected basically with disturbances of the vegetative [autonomic] nervous system; hot-flushes, chills, dizzy spells, cold, moist or numb extremities, tachycardia, palpitation, dyspnea, headaches, sweating and formication. Contributed to by the vegetative imbalance there are also disturbances of all the other body systems, which sometimes become the major source of trouble."



NEURO-CIRCULATORY SYMPTOMS

Kavinoky[2] believes that ". . . in the management of menopausal disorders, three possibilities are kept in mind: (1) stabilization of the hormonal imbalance, (2)stabilization of the autonomic imbalance, and (3) psychotherapy.

GLANDULAR IMBALANCE

"The most logical approach is to consider all three, with emphasis upon re-establishment of the autonomic nervous system balance. This is obtained with the simultaneous administration of drugs which inhibit cholinergic and adrenergic stimuli. Such drugs might include Bellergal,® each tablet containing 0.3 mg. Gynergen® (ergotamine tartrate) to inhibit the adrenergic stimuli; Bellafoline,® (levorotatory alkaloids of belladonna) 0.1 mg. to inhibit cholinergic stimuli; and phenobarbital 20.0 mg. to provide sedation of the higher centers of autonomic regulation in the brain stem. The combination of these drugs makes it possible to obtain sedation of the entire autonomic nervous system."

OVARIAN DYSFUNCTION

Clinical Results

This study[2] deals with the results obtained with Bellergal in the treatment of 125 women who presented climacteric symptoms. Following a complete physical examination, "Each patient was given from three to five Bellergal® tablets daily for two to four weeks. If the symptoms were not relieved by three tablets, two more were added at bedtime or at the time of day when the patient was most disturbed. No estrogens were given during the initial period of treatment. Vitamins and thyroid extract were prescribed and an interpretation of the climacteric was given. The psychotherapy has more effect after the patient becomes stabilized.

"Of the 125 patients treated, 73 responded so well that the dose was reduced to one to two tablets at bedtime for another week or two, or the drug was completely discontinued. Some now only take a few tablets to help them through critical situations.

continued

The preceding data shows . . .

THE CLIMACTERIC AT ITS CLIMAX,
REQUIRES EMOTIONAL ADJUSTMENT . . .

- ***Results obtained with BELLERGAL® in the treatment of Menopausal Symptoms***[2]

SYMPTOMS	NO. PATIENTS	RESULTS			
		E	G	F	P
FLASHES	92	78	7	1	6
SWEATS, NERVOUSNESS, TACHYCARDIA	61	31	18	4	8
HEADACHE, DIZZY SPELLS	43	22	5	6	10

E — *Excellent* G — *Good* F — *Fair* P — *Poor*

Kavinoky[2] concludes that:

1. The vegetative nervous system plays an important role in the menopause syndrome.
2. Bellergal® is a safe and reliable sedative of the autonomic nervous system.
3. Bellergal proved to be a useful adjunct in the treatment of 125 patients with various menopause disturbances.

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DISTURBED AUTONOMIC PHYSIOLOGY
in the Menopause

PROBLEM: Under New York law, a suit for malpractice must be brought within two years from the date when right to sue begins unless the doctor is absent from the state for a year or longer. A doctor living in New Jersey maintained an office in New York which he attended daily and where he treated a patient. Could the two-year period be extended in these circumstances?

COURT'S ANSWER: No.

The New York Supreme Court, Special Term, Nassau County, in effect declared that a doctor living in one state but maintaining his office in another is not to be deemed "absent" from the state for the purposes of computing the time within which summons may be served upon him (116 N. Y. Supp. 2d 667).

PROBLEM: A clinic was operated under a partnership agreement, one paragraph of which provided that if a partner should withdraw he should assign his interest to his associates and they should pay him its value. A separate paragraph provided that if a partner should retire at the request of his associates, he should be paid the value of his interest, plus two and one-half months salary "from and after the date of notice" of requested retirement. A partner withdrew voluntarily to join a clinic in another city. Was he entitled to two and one-half months salary?

COURT'S ANSWER: No.

The Texas Court of Civil Appeals, Fort Worth, ruled that this was a fair interpretation of the contract, because the provision for salary appeared only in the paragraph dealing with involuntary retirement and because there was naturally more reason for such allowance in case of involuntary, rather than voluntary, retirement (252 S. W. 2d 201).

AN IMPORTANT CONTRIBUTION IN THE ERADICATION OF

*Trichomonas Vaginalis Vaginitis**

SYMPTOMATIC RELIEF *in 1/3 the time*
CULTURE-ESTABLISHED CURE *in 1/3 to 1/2 the time*

* Shaw, H. N.; Henriksen, E.; Kessel, J. F., and Thompson, C. F.: Clinical and Laboratory Evaluation of "Vagisol" in the Treatment of Trichomonas Vaginalis Vaginitis, Western J. of Surg., Obst. & Gynec. 60:563 (Nov.) 1952.

Plus a 98% cure rate

In a recently reported study,* 100 patients with proved trichomonas vaginitis were given 36 Vagisol Suppositabs (tablet-shaped suppositories), with instructions to insert one each morning and night well up into the vaginal vault, regardless of intervening menstruation.

In the control group, 40 patients were treated with another widely used medication.

All patients, subjects as well as controls, were asked to return after 3 weeks. Effect of medication was checked by every accepted laboratory procedure, including parasitologic culture. If the patient was found negative by all methods used, complete biweekly rechecks were done over a period of 10 weeks, before she was discharged as cured.

The remarkable superiority of Vagisol was demonstrated by these significant findings:

A 98% cure rate (98 out of 100) in the Vagisol treated group.

Under Vagisol therapy patients were symptom-free after 2.15 mean patient days. *For the control group, 6.75 mean patient days were required to render them symptom-free.*

72% of the patients in the study group were cured in 18 days, 22% in 36 days, 4% in 54 days. *In the control group 25% required 56 days of therapy, 42.5% 84 days, and 20% required 112 days for culture-demonstrable cure.*

The desirable clinical behavior of Vagisol is due to the powerful antibacterial and antiparasitic actions of phenylmercuric acetate and tyrothricin, the digestant action of papain, the surface activity of sodium lauryl sulfate, and the pH reducing influence of lactose and succinic acid.

Each Vagisol Suppositab, odorless and nonstaining, contains:

Phenylmercuric Acetate	3.0 mg.
Tyrothricin	0.5 mg.
Succinic Acid	12.5 mg.
Sodium Lauryl Sulfate	3.0 mg.
Papain	25.0 mg.
Lactose	0.75 Gm.

Vagisol Suppositabs, supplied in bottles of 36, are available on prescription through all pharmacies. Physicians are invited to send for literature and clinical test samples. Please address Smith-Dorsey, a Division of The Wander Co., Lincoln, Nebraska.

VAGISOL

A DORSEY PREPARATION

PROBLEM: A doctor was sued for alleged malpractice in treating fractured tibia and fibula. The plaintiff relied upon an 82-year-old gynecologist as a witness to establish defendant's negligence, although the gynecologist had not operated for twenty years and within that time had only occasionally observed operations. The trial judge ruled that the proposed witness was not qualified to testify and dismissed the suit for lack of medical testimony to show negligence. Should the aged specialist have been permitted to testify?

COURT'S ANSWER: Yes.

In ordering a new trial, the New Jersey Superior Court, Appellate Division, decided:

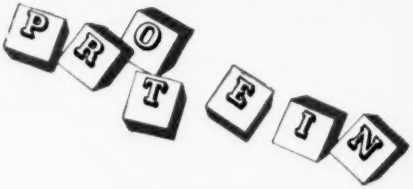
As to defendant's liability to the patient, the degree of care and skill exacted by the law depended upon whether defendant was a specialist in treating fractured legs or merely a general practitioner. As a specialist he would be required to use the care and skill normally used by such specialists in his community, as distinguished from that used by general practitioners. There being nothing to show whether he was a specialist or general practitioner, it would be presumed in his favor that he was the latter.

As to qualifications of witnesses, a doctor need not be a specialist in the field involved, but, if he is not, that fact may be considered by the jury in determining what weight should be given to his opinions.

The mere fact that a doctor offered as a prospective witness holds a license to practice does not establish his qualifications to testify to a medical opinion on a given point of practice. He must know by experience or study what constitutes proper practice.

If there is reasonable doubt as to qualifications the doctor should

Knox Gelatine... useful protein supplement for the growing child



For Body Growth

Protein not only helps feed the machine of the growing child but is itself the machinery. An abundance of protein both for body growth as well as for blood, enzyme and hormone synthesis is a primary requirement in childhood. While carbohydrate and fat may be stored in the organism, protein must be taken in daily to maintain the structural mass of tissue.

Abundant Energy

The daily diet must contain the so-called essential amino acids as first shown by Osborne and Mendel[1] and more precisely defined by Rose.[2] Once the essential amino acids are furnished, the remaining ones may be taken in abundance from other protein sources to insure full growth and create abundant energy.

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Easy to Digest

Knox Gelatine is an excellent protein supplement, easy to digest and administer, and non-allergenic. It may be prepared in a variety of ways from Knox Gelatine Drink to delicious salads and desserts.

High Dynamic Action

Gelatine in the form of gelatinized milk has been found a valuable protein supplement helpful in allergies, celiac disease, colic and to increase the digestibility of the milk formula.[3] Its high specific dynamic action[4] which spares essential amino acids and furnishes amino acids for the continuous dynamic exchange of nitrogen in the tissue[5] helps the child to maintain the normal body heat. Furthermore, it contains an abundance of important glycine and proline necessary for hemoglobin formation.

1 Osborne, T.B. and Mendel, L.B., J. Biol. Chem. 17:325, 1914.
2 Rose, W.C., Physiol. Rev. 18:109, 1938.
3 Wolpe, Leon Z. and Silverstone, Paul C., J. Pediat. 21:635, 1942.
4 Lusk, G., J. Nutrition 3:519, 1931. Borsook, H., Biol. Rev. 11:147, 1936.
5 Schoenheimer, R., Ratner, S., and Rittenberg, D., J. Biol. Chem., 127:333, 1939 and 130:703, 1939.

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be permitted by the trial judge to testify, balancing preservation of the right of injured persons to reasonable opportunity to establish their claims in court and the difficulty that is commonly met in securing as expert witnesses doctors who are willing to testify against brethren in malpractice suits.

This witness should have been permitted to testify, subject to cross-examination, as to his knowledge and experience and to the jury's right to determine what weight should be given to his opinions (91 Atl. 2d 540).

PROBLEM: A doctor's offices were located in a large and much used medical arts building. A door opening into the lobby was defective because of improper adjustment of door-check mechanism. The door could also be regarded as a hazard to users because of its location and lack of a guard rail. The doctor's head nurse was seriously injured through violent opening of the door as she stood nearby. Was the operator of the building liable to her in damages?

COURT'S ANSWER: Yes.

The Texas Supreme Court applied the general rules of law that the owner or operator of premises used by business visitors and other invitees is bound to use reasonable care to keep the premises in safe condition but owes no duty to one who is as fully aware of a dangerous condition as the owner or operator. Judgment in favor of the plaintiff was upheld on the ground that the evidence was such that it was for the jury to decide whether defendant had more knowledge than plaintiff as to the danger involved in use of the door, and whether plaintiff used due care for her own safety (251 S. W. 2d 497).

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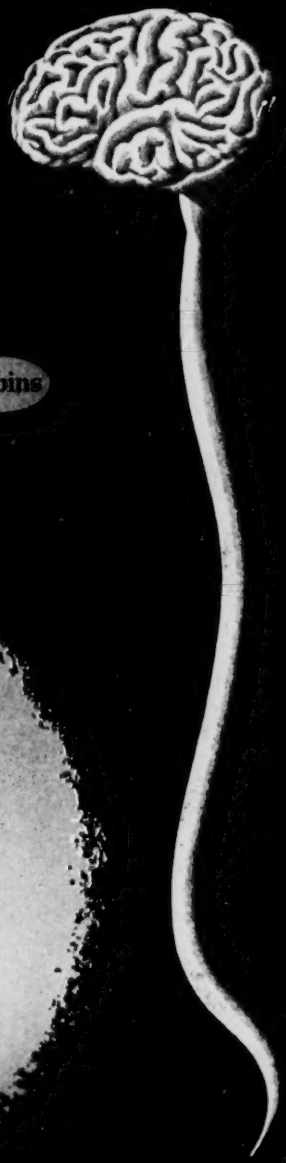
Robins



In Mephate 'Robins', the clinical usefulness of mephenesin per os has been significantly heightened by the inclusion of glutamic acid hydrochloride, which improves absorption and enhances effectiveness for many patients otherwise unresponsive.* Provides a relaxant effect on skeletal muscle spasm; an ameliorating effect on tremor; and a relief of anxiety without dimming consciousness. Particularly helpful in abnormal neuro-muscular conditions such as rheumatic disorders, disc syndromes and cerebral palsy; alcoholism, anxiety tension states and psychiatric states.

In each Mephate Capsule, 0.25 Gm. mephenesin — with 0.30 Gm. glutamic acid hydrochloride. Adult dosage starts at 2 capsules 3 or 4 times a day, preferably with food or liquids.

*Hermann, I. F., and Smith, R. T.: JL.- Lancet 71:271 (July), 1951.

Washington LETTER

Lady from Texas Promises a 'Few Changes' in FSA

The demure new administrator of Federal Security Agency, Mrs. Oveta Culp Hobby, already has made it abundantly clear that she is not satisfied with the status quo and that there'll be some changes made.

She had hardly rearranged the furniture in the administrator's office when she let it be known publicly that she is in Washington neither to carry on just the way her predecessor had, nor to wreck what the Democrats had done in health and welfare over the last twenty years.

Mrs. Hobby

Addressing a group of Republican women in Washington, Mrs. Hobby said that quite a few of the social changes effected by the Democrats had her and her party's blessing, and that she would not take part in any campaign to disturb them. At the same time she said that the whole health-welfare-educational structure of her agency would be studied and that where improvements could be made they would be made, definitely and thoroughly. She declared:

> To junk at once all that came to us from the preceding administration would be unfair. . . . In our eagerness to improve our federal government and our national situation, we must not start with any idea that the policy can be changed overnight. . . . The question is what to save, what to modify, what to change radically.

Later, at a series of staff meetings, Mrs. Hobby told FSA employees not to worry about their jobs—but at the same time she indicated they shouldn't be surprised, after the passage of time, if they noticed a few changes.

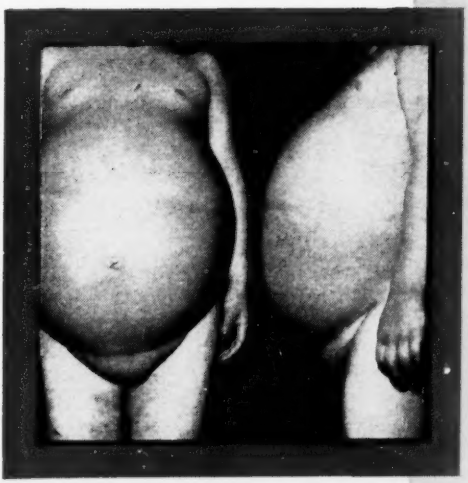
The Senate committee that went through the motions of examining

(Continued on page 60)

moderation for variation..

in the blended diuretic regimen

In the long-term regimen, Calpurate meets the clinical need for moderate diuretic action, sustained effectiveness, and minimal toxicity. Calpurate also promotes increased cardiac output.



Calpurate is the chemical compound, theobromine calcium gluconate... unusually free from gastrointestinal and other side effects... does not contain the sodium ion.

to 'lighten the load' in congestive heart failure

Calpurate is particularly indicated:

when edema is mild and renal function adequate...

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for moderate, long-lasting diuresis in chronic cases.

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SUPPLIED: Calpurate Tablets of 500 mg. (7½ gr.)
Calpurate Powder
Calpurate with Phenobarbital Tablets—16 mg. (¼ gr.) phenobarbital per tablet

Resion . . . *for more rapid, more complete control of*

DIARRHEA . . . INFANTS AND ADULTS

NAUSEA OF PREGNANCY

FOOD POISONING

ENTERIC INFECTIONS

Mrs. Hobby's fitness for the job must have been quite reassuring to her.

Waiting her turn as a witness, she watched and heard Mr. Eisenhower's selection for head of the Treasury subjected to more than an hour of close questioning. His income, bonuses, stock holdings, and business connections were drawn out on the public record for all to see. In the end, he was approved unanimously, but Mr. Humphrey knew he had been to a hearing.

Mrs. Hobby was before the committee for about ten minutes. First, the chairman went around the horseshoe presenting the committee members to her. Then, following the reverse order, he allowed the members to make a few remarks. What followed was something unusual, even for senators skilled in flowery language and gracious gestures. Typical was Sen. Kerr of Oklahoma. "Mrs. Hobby," he said, "I wouldn't in the least question your fitness for this important position. My differences with you concern only differences between the great states of Oklahoma and Texas, differences which I think we can settle at a forum other than this one."

And so it went.

Mrs. Hobby had thoughtfully provided herself with mimeographed statements carefully listing her financial dealings and holdings. The pages were fairly heavy with stock, real estate, and industrial properties. They showed, without any question, that she could be considered approximately a millionairess. Nor were the admiring senators the ones to ask any questions.

The reception was in sharp con-

(Continued on page 64)

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NON-BARBITURATE
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TASTELESS
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3¾ gr.
Daytime sedation – *without hangover*

7½ gr.
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Available – 3¾ gr. (0.25 Gm.), bottles of 24's and 100's
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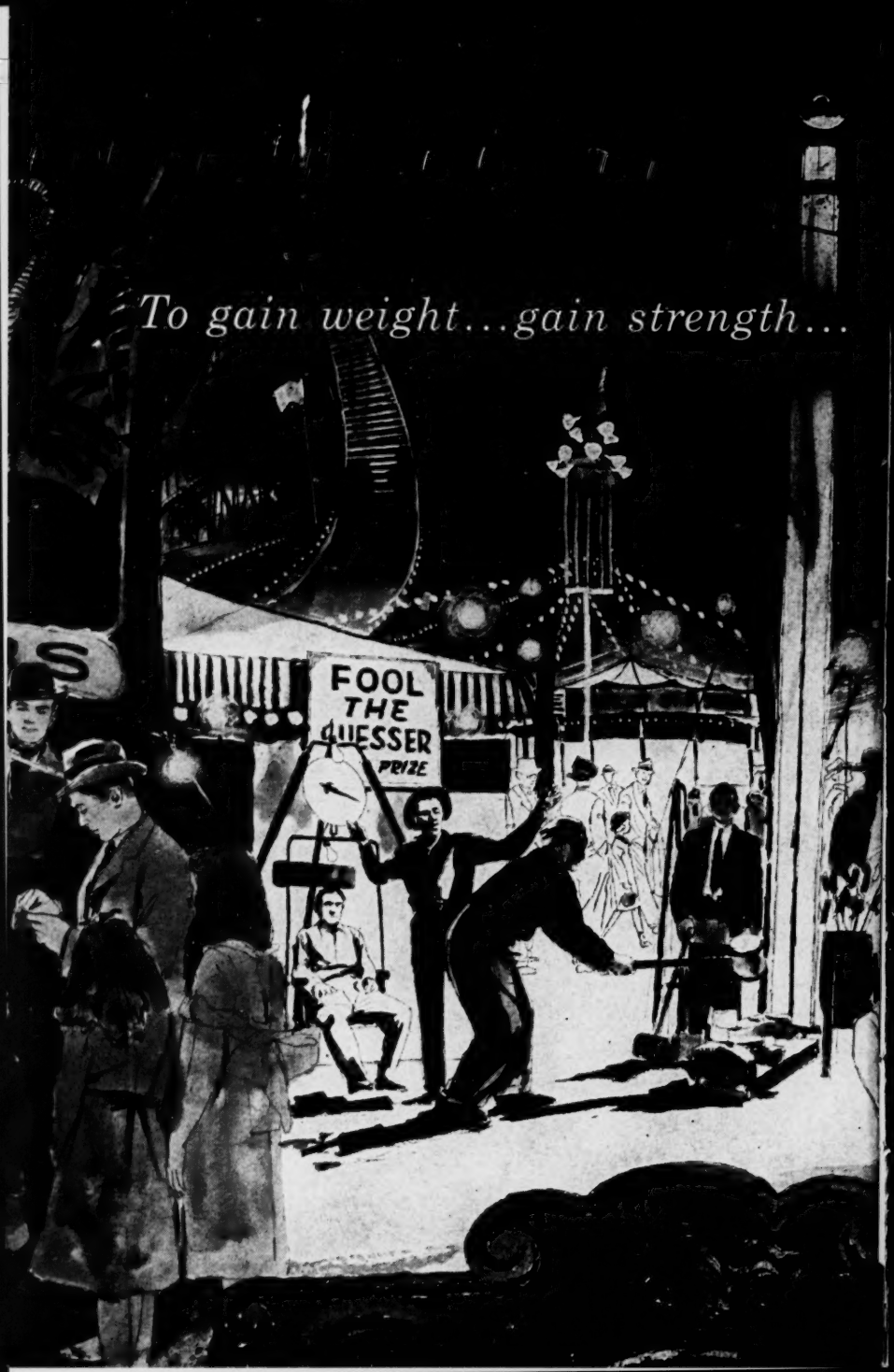
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A highly palatable emulsion containing 50 percent coconut oil and 12½ percent sucrose, useful whenever caloric intake must be increased without undue increase in bulk.

Delicious alone, or when taken with milk and other fluids, semisolid foods, and desserts.

EDIOL* furnishes 600 calories daily, when taken as 2 tablespoonfuls q.i.d. The unusually small particle size of EDIOL (average, 1 micron) favors easy digestion, rapid assimilation.

For children, or where fat tolerance is a problem, small initial dosage may be prescribed, then increased to the level of individual capacity.

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trast to the usual experiences of Mrs. Hobby's predecessor as FSA administrator, Oscar Ewing. Not even on the finest day, with the issue noncontroversial and the weather balmy, could Mr. Ewing hope to escape. If the exchanges were limited to senatorial satire, Mr. Ewing was indeed fortunate. His espousal of national compulsory health insurance, long after it was apparent Congress didn't want it, had made him a standing target.

From the start of her tenure, Mrs. Hobby enjoyed unusual support from her superior, President Eisenhower. He very soon made it known that he thought the Federal Security Agency might well be raised to a cabinet department, and Mrs. Hobby made a full-ranking member of the cabinet. Here President Eisenhower and Mrs. Hobby were boldly moving into a knotty problem. Repeatedly in other years the Democratic administration had proposed this change. And repeatedly Congress had voted it down. The trouble was that representatives of the nation's medical and educational professions had opposed this type of grouping; each argued that its field was deserving of a cabinet post of its own.

There is now, of course, the possibility that a compromise can be reached, with the interests of both medicine and education adequately protected in the new department. In fact, the prospects for agreement are pretty favorable; neither profession is suspicious of the Eisenhower administration, the way medicine particularly was of both Roosevelt's and Truman's.

Regardless of future developments, when President Eisenhower proposed creation of the new cab-


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Now thoroughly evaluated in many thousands of successful therapeutic trials, BICILLIN takes its place as an outstanding form of the basic antibiotic, penicillin

BICILLIN brings to penicillin therapy new dimensions of reliability . . . of persistence of blood levels . . .

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Fluid oral penicillin that is effective, palatable, stable, ready to use

Oral forms that do not require a buffer against gastric juices; are taken regardless of mealtimes without loss of potency

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inet post one question mark immediately was removed: Mrs. Hobby had not come to Washington to preside meekly over Federal Security Agency. She is here to do a job. Only time will tell whether, in this role, the senators will still find her the same fascinating little woman from Texas.

One of the things Mrs. Hobby will be concerned with shortly will be a redirection of emphasis from the federal government to states in health and welfare programs. Throughout the election campaign Gen. Eisenhower promised an extension of health and security programs—but it sometimes is forgotten that just as consistently he argued that the federal government was assuming too much and the states too little responsibility in these fields.

Doctors often are inclined to assume that there is little day-to-day relationship between federal grants and their own medical practice. Actually, the ties are very close. Next to the grocer and the landlord, the doctor is more affected than anyone else by these federal dollars and the federal control that accompanies them. Usually he doesn't recognize the regulatory hand reaching out from Washington, because he deals with state representatives, but the hand is there just the same.

Federal funds flow out to states under several programs, and in all of them the medical profession is intimately involved. The total is more than a billion dollars, an amount well in excess of combined state and local spending in these fields.

The largest category is old age assistance, or relief, including di-

rect payments to physicians for medical care of the indigent aged.

Aid to dependent children makes up the second largest item.

Aid to the blind is a much smaller figure, but an operation in which physicians are deeply involved.

The newest program—assistance to the permanently and totally disabled—involves doctors originally in determining disability, then continuously in treating the disabled.

Various formulas are used to pass the money on to the states, but the objective always is to offer states bargain programs, through which, for a small amount of its own money, the state can get a large amount of federal money.

The state-U. S. conflict originates in the requirement that some federal official has to watch over the spending of every federal dollar. Thus a degree of control is forced on the states. Objection of state medical and welfare officials to this growing pattern of regulations is coming to a head in this Congress.

A recent study by the Tax Foundation of New York City attempts to analyze and centralize these complaints. High on the list was a demand that the amount of federal supervision be decreased. Another important grievance was expressed against the present system of earmarking most federal dollars, that is, not allowing the state to use for the totally and permanently dis-

(Continued on page 236)

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the complete lipotropic therapy

...because it provides vitamin B_{12} and liver fractions in addition to choline, methionine and inositol.

...helps normalize liver function, increase phospholipid turnover, reduce fatty deposits, and stimulate regeneration of new liver cells...

...helps reduce elevated cholesterol levels and chylomicron ratios towards the normal, and aids in achieving normal fat metabolism.

the suggested daily therapeutic dose of 9 capsules or 3 tablespoonfuls of Methischol provides:

Choline Dihydrogen Citrate*	2.5 Gm.
dl, Methionine	1.0 Gm.
Inositol	0.75 Gm.
Vitamin B_{12}	18 mcg.
Liver Concentrate and Desiccated Liver**	0.78 Gm.

*Present in syrup as 1.15 Gm. Choline Chloride
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now — higher B_{12} potency

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two forms:
2 cc. ampuls for intramuscular use,
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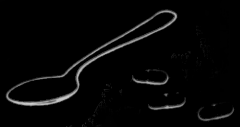
for use when oral therapy is impractical or impossible.



condition	*incidence of blood lipid abnormalities*	*suggested therapy*
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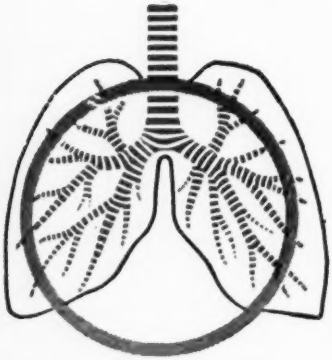

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(1) Bordley, J. E., et al.: Bull. Johns Hopkins Hosp. 85: 396, 1949; (2) Rose, B., et al.: Canad. M. A. J. 62: 6, 1950; (3) Randolph, T. G., and Rollins, J. P.: In Proceedings of First Clinical ACTH Conference, edited by J. R. Mote. Philadelphia, The Blakiston Co., 1950, p. 479; (4) McCombs, R. P., et al.: Bull. New England M. Center 12: 187, 1950; (5) Baldwin, H. S., and DeGara, P. F.: J. Allergy 23: 15, 1952; (6) McCombs, R. P.: New England J. Med. 247: 1, 1952.

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Three Servings of Ovaltine in Milk Recommended for Daily Use Provide the Following Amounts of Nutrients

(Each serving made of ½ oz. of Ovaltine and 8 fl. oz. of whole milk)

MINERALS		VITAMINS	
*CALCIUM	1.12 Gm.	*ASCORBIC ACID	37 mg.
CHLORINE	900 mg.	BIOTIN	0.03 mg.
COBALT	0.006 mg.	CHOLINE	200 mg.
*COPPER	0.7 mg.	FOLIC ACID	0.05 mg.
FLUORINE	3.0 mg.	*NIACIN	6.7 mg.
*IODINE	0.15 mg.	PANTOTHENIC ACID	3.0 mg.
*IRON	12 mg.	PYRIDOXINE	0.6 mg.
MAGNESIUM	120 mg.	*RIBOFLAVIN	2.0 mg.
MANGANESE	0.4 mg.	*THIAMINE	1.2 mg.
*PHOSPHORUS	940 mg.	*VITAMIN A	3200 I.U.
POTASSIUM	1300 mg.	VITAMIN B_{12}	0.005 mg.
SODIUM	560 mg.	*VITAMIN D	420 I.U.
ZINC	2.6 mg.		

*PROTEIN (biologically complete)	32 Gm.
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FERROUS SULFATE U.S.P.	4.5 gr.
VITAMIN B12	5.0 mcg.
FOLIC ACID	0.33 mg.
ASCORBIC ACID	50.0 mg.
COBALT	0.1 mg.
COPPER	1 mg.
MOLYBDENUM	0.2 mg.
CALCIUM	37.4 mg.
IODINE	0.05 mg.
MANGANESE	0.033 mg.
MAGNESIUM	2 mg.
PHOSPHORUS	29.0 mg.
POTASSIUM	1.7 mg.
ZINC	0.4 mg.
VITAMIN A	5,000 U S P UNITS
VITAMIN D	500 U S P UNITS
THIAMINE HYDROCHLORIDE	2 mg.
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PYRIDOXINE HYDROCHLORIDE	0.1 mg.
NIACINAMIDE	10 mg.
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HEPTUNA PLUS supplies ALL the Vitamins, Minerals and Trace Elements needed to increase and maintain erythrocyte and hemoglobin levels.

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He can make words sing, soar, rumble or smash, as his purpose serves—but they serve him no purpose when he writes of a balanced diet. Soon, his doctor will pen him a prosaic but startling headline: *Avitaminosis* B—along with a story of corrected diet plus Sur-bex or Sur-bex with Vitamin C. Note the potent formula.

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Try them with your "Dietary Dubs." Abbott

each triple-coated SUR-BEX Tablet contains:

Thiamine Mononitrate (6XMDR*)	6 mg.
Riboflavin (3XMDR*)	6 mg.
Nicotinamide (2XRDA†)	30 mg.
Pyridoxine Hydrochloride	1 mg.
Vitamin B_{12} (as vitamin B_{12} concentrate)	2 mcg.
Pantothenic Acid (as calcium pantothenate)	10 mg.
Liver Fraction 2, N.F.	0.3 Gm. (5 grs.)
Brewer's Yeast, Dried	0.15 Gm. (2½ grs.)

Sur-bex with Vitamin C contains 150 mg. of ascorbic acid (5XMDR*) in addition to the vitamin B complex factors above.

*Minimum Daily Requirement
†Recommended Daily Dietary Allowance

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losing ground at last

A Modern Medicine Editorial

For years, laboratory workers avoided conflicts with the antivivisectionists and fought back only when attacked. While the pounds in every city were charging the taxpayers for destroying thousands of stray dogs, laboratory workers were having to pay out of their small funds large amounts for animals.

Commonly these animals were bought from pounds in cities far from the laboratory, but the antivivisectionists always kept snooping until they found whence the animals were coming and then put such pressure on the poundmaster that he no longer dared to sell the animals.

That the antivivisectionists hate not so much cruelty to animals as progress in medicine was clearly shown when they blocked the efforts of a distinguished research worker to buy the pituitary glands of dead dogs which the city pound was selling by the hundreds to a fertilizer works! In this case the president of the Humane Society, a sensible man, would gladly have given the dead dog's heads to the university but he did not care to fight it out with his "lunatic fringe."

In recent years the research laboratories have been carrying the war to the enemies' camp. They have demanded the right to buy unclaimed strays from the local pounds and, in several states, they have won hands down. They have won referendums held even in cities which are hotbeds of antimedical sentiment.

As an article in *Collier's* pointed out, one big reason for the large majorities rolled up in favor of experimental medicine was the insane behavior of the antivivisectionists. Thus, in a poll conducted in Philadelphia, 4 out of 5 antivivisectionists who were parents said that they would not sacrifice a dog to save their children, and 100% of the antivivisectionists who were not parents said that they would sacrifice a child any day rather than a dog!

During the years in which I fought antivivisectionists, I often heard them make such statements. I remember the president of an antivivisectionist society who said at a public hearing that her two children had died of diphtheria, and she was proud that in losing them she had not dragged down any animal to its death! In Baltimore the antivivisectionists hurt their cause by booing a little girl whose life had been saved by a Blalock operation.

Once, after a legislative hearing where I had spoken in favor of research, a young woman buttonholed me and, with blazing eyes and vitriolic tongue, told me that man had no right to use animals in any way against their will. I laughed and said, "You, in your full-length wild mink coat, are a fine one to talk. How many dozen little animals do you think were caught in a cruel trap and allowed to die slowly of pain and hunger and cold in order that you might look chic?" The crowd laughed; the girl blushed, stammered, and slunk off.

WALTER C. ALVAREZ

Let Us Not Drown Patients

Yesterday an able physician said sadly, "I think my brother drowned at the hospital. He drowned in 6 liters of intravenously given fluid which he did not need because at his operation he did not lose much blood. The liquid was ordered thoughtlessly and the order was not countermanded. His lungs suddenly frothed up and he died. The pathologist says he has seen many similar cases."—W.C.A.

Substantial transient enlargement of intrathoracic lymph nodes can occur without associated symptoms.

Transient Thoracic Lymphadenopathy

AARON D. CHAVES, M.D., AND HANS ABELES, M.D.
New York City Department of Health

ONE of the most common forms of lymphadenopathy encountered in routine chest examination of apparently healthy adults is enlargement of mediastinal nodes that subsides in a few months without symptoms or other sign of illness.

To exclude more serious conditions, a thorough examination and, at times, thoracotomy should be done, but so-called diagnostic irradiation is ill-advised. Whether benign lymphadenopathy represents a variant of sarcoidosis, tuberculosis, infectious mononucleosis, erythema nodosum, mycosis, or other disease requires further investigation.

Aaron D. Chaves, M.D., and Hans Abeles, M.D., found 20 cases of transient benign enlargement in records from tuberculosis surveys and 23 chest clinics. A definite diagnosis could not be established because biopsy of superficial glands and chest operation were refused.

However, physical examinations were done, and several laboratory tests were completed. Serial roentgenograms were made of the thorax, and also views of the hands. In 8 instances, normal chest films had been obtained three months to five years earlier.

All subjects but 1 were 19 to 31 years old; 15 were white and 5 Negro. All had lived in the city for a long time without occupational exposure or signs of allergy. None knew of a previous illness or recent contact with infectious disease.

Lymphadenopathy obviously involved both sides of the chest in 16 cases. In every instance, some intrathoracic nodes were greatly enlarged, and in 6, peripheral glands were slightly affected.

Location of swollen glands varied considerably. The hilum was always involved, but nodes were seen near, below, or above root structures, and 7 patients had paratracheal lesions. Cutaneous reactions to 1 mg. of old tuberculin were negative in 10 of 19 cases.

In 11 persons seen at frequent intervals, lymphadenopathy disappeared in two and one-half to nine months. The entire group remained in good health throughout observation, for one to nearly ten years, with an average period of five years.

Large intrathoracic lymph nodes call for intensive examination, including biopsy of peripheral glands, when possible, and the Kviem test. If the diagnosis remains obscure and enlarged nodes are unilateral,

Transient undiagnosed intrathoracic lymphadenopathy in apparently healthy persons. Am. Rev. Tuberc. 67:45-58, 1953.

the chest should be opened promptly. In the same exploratory procedure, a resectable cancer or lymphoma may be removed.

Although bilateral lesions cannot be excised, a diagnostic operation should be done fairly soon, if the physician believes that certain lymphomas respond to early intensive irradiation.

The effects of supposedly diagnostic radiation do not actually distinguish benign from malignant growth and may conceal spontaneous shrinkage. The chance of natural recovery should be kept in mind also when cortisone, ACTH, or antibiotics are given for unexplained intrathoracic lymphadenopathy.

Oral Protoveratrine for Hypertension

S. W. HOOBLER, M.D., R. W. CORLEY, M.D.,
T. G. KABZA, M.D., AND H. F. LOYKE, M.D.

A PURIFIED derivative of *Veratrum album*, protoveratrine, may reduce high blood pressure for six to eight hours daily without producing nausea or drug tolerance.

The drug is most useful in therapy of ambulatory patients when other methods are unsuitable or inadequate. Treatment is palliative only. Serious manifestations may be relieved, including hypertensive heart failure, retinopathy with poor vision, impending cerebral hemorrhage, and severe headaches.

Hypertension from such varied diseases as poliomyelitis, chronic nephritis, toxemia of pregnancy, and malignant nephropathy may respond. From 10 to 20% of patients are refractory or hypersensitive to emetic action, however.

Protoveratrine is not given to patients with advanced azotemia, unless manifestations listed are dominant, with extreme arteriosclerosis, or after recent cerebral thrombosis.

A strict schedule is necessary, explain S. W. Hoobler, M.D., R. W. Corley, M.D., T. G. Kabza, M.D., and H. F. Loyke, M.D., of the University of Michigan, Ann Arbor.

At 8 A.M., immediately after breakfast, 0.5 to 1.5 of protoveratrine is administered by mouth and 0.25 mg. at 10 A.M. and 1 P.M. Tablets must be taken after meals or not less than one and one-half hours before eating. For paroxysmal nocturnal dyspnea, treatment starts after the evening meal.

Since dosage may need to be changed, therapy is reviewed every two to four weeks in the clinic, with observation every half hour throughout the day.

Treatment of hypertension with oral protoveratrine. Ann. Int. Med. 37:465-481, 1952.

Symptoms of occlusion of the aorta depend on the rapidity of development of the occlusive process.

Gradual Thrombotic Closure of the Aorta

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University of Texas, Dallas

WARREN W. MOORMAN, M.D.
St. Joseph Hospital, Fort Worth

THROMBUS of the aortic bifurcation may ultimately progress to the stage of complete obstruction.

In contrast to the sudden severe pain of saddle embolus, symptoms usually develop insidiously and often continue for years. The most frequent cause is atherosclerosis, and more than 90% of patients are men.

Diagnosis can be confirmed by arteriography with little risk. In some cases, however, coarctation of the aorta or occlusive vascular disease is suspected, and the lesion is not identified until after death.

Underlying vascular sclerosis or propagation of the thrombus is generally fatal, although recent surgical technics offer considerable hope. Peripheral circulation may be improved by upper lumbar ganglionectomy.

William E. Barnett, M.D., Warren W. Moorman, M.D., and Ben A. Merrick, M.D., describe 6 cases of gradual aortic thrombosis with symptoms averaging more than six years. Only 2 cases were identified during life, neither in time for effective treatment.

The condition usually develops in the fourth to sixth decade, and the clot is frequently attached to ulcerated atherosclerotic plaques. Other predisposing factors are arteriosclerotic, syphilitic, or dissecting aneurysm, trauma to the lower abdomen, uterine or spinal tumor, and in babies, umbilical sepsis.

Manifestations depend on the rate of circulatory occlusion. The process may be so gradual that collateral vessels develop and provide a fairly adequate blood supply to the lower extremities. In other instances, acute arterial insufficiency occurs in various degrees.

The chief symptoms may be weakness and weariness of the legs, painful cramps on walking or, in some cases, both easy fatigability and intermittent claudication. Sexual potency may be impaired. Arterial tension in the arms is often though not always high.

Extreme pallor of legs and feet is seen on elevation of the limbs, sometimes when the patient is standing. Ordinarily, aortic pulsations are not palpable in the abdomen except high above the umbilicus, and no beat is felt in or below the thighs. However, large anasto-

Thrombotic obliteration of the abdominal aorta: a report of six cases. Ann. Int. Med. 37:944-965, 1952.

moses may produce femoral pulsations on either or both sides, and occasionally blood pressure may be recorded below the obstruction.

At times, the lower extremities become atrophic without obvious lesions. The late stage of thrombosis may cause cyanosis, desquamation of the skin, ulcers at pressure points, and extreme pain. Gangrene frequently necessitates amputation of one or both limbs.

In spite of a subtle onset often complicated by more evident disease, obliterative thrombosis has several points of difference from similar types of circulatory obstruction:

- Coarctation of the aorta is commonly excluded by roentgen appearance of a normal arch, calcification of the abdominal aorta, and absence of rib notching, though subdiaphragmatic coarctation may require radiographic study for differentiation.
- Arteriosclerosis obliterans occurs at more advanced ages, with relatively early trophic changes and gangrene. Pulsations are felt in the entire abdominal segment of aorta, and sclerotic lesions may be detected in the dorsalis pedis artery.
- Thromboangiitis obliterans is associated with phlebitis, pain occurs much sooner, and rubor with dependency is usual.
- Aneurysm of the abdominal aorta generally forms a pulsatile tumor that frequently erodes the spine.

¶ NONTOXIC GOITERS may be reduced in size and the euthyroid state be established in myxedematous patients by oral administration of l-thyroxine sodium. The compound suppresses the uptake of radioactive iodine by the normal gland. The dosage used by Solomon Papper, M.D., and associates of Harvard University, Boston, is 0.1 mg. of the hormone daily initially, increased by 0.1 mg. every four weeks if necessary, for goitrous subjects; and 0.05 to 0.1 mg. daily in cases of untreated myxedema, increments of 0.1 mg. being added as the response is stabilized. The ingested drug is comparable in effect to glandular extract given by mouth. Elthrin, the synthetic preparation employed, is equivalent to thyroid, U.S.P., in the ratio of 0.1 mg. to 0.06 gm. (1 gr.), and contains 65 μg. of iodine.

New England J. Med. 247:897-899, 1952.

¶ ACUTE PERICARDITIS is most frequently a sequel to rheumatic fever. Robert L. Reeves, M.D., found this causal relationship in 40.6% of 96 cases of the cardiac condition diagnosed at St. Luke's Hospital, New York City, between 1935 and 1950. Purulent, tuberculous, and benign infections accounted for 19.8%, 7.3%, and 10.4%, respectively. Noninfectious causes were uremia, 11.5%; neoplasm, 3.1%; and the so-called collagen diseases, 2.1%.

Am. J. M. Sc. 225:34-38, 1953.

Laboratory data make diagnosis of pancreatitis possible early enough for judicious medical management.

Diagnosis of Pancreatitis

IRVING INNERFIELD, M.D.
New York Medical College, New York City

CONSISTENTLY elevated antithrombin titers are a diagnostic criterion for acute pancreatitis.

Since the antibody response follows closely the clinical course, the antithrombin determination has diagnostic and prognostic significance even when determined at intervals varying from three hours to two weeks after onset of the disease. This is in contrast to serum amylase, which is rarely of value longer than twenty-four hours after appearance of symptoms.

Because the initial symptoms of pancreatic disturbance are often slight, the disorder is seldom recognized before the appearance of agonizing abdominal pain, ashy cyanosis, and shock. Yet diagnosis may be achieved in cases of persistent upper abdominal pain by the simple expedient of drawing a sample of blood during or shortly after an attack for determination of antithrombin titer and concomitant serum amylase studies. By use of precise laboratory aids, early diagnosis is possible when judicious medical management may be used. Such therapy yields the best results in early cases except with suppurative pancreatic disease.

Antithrombin appears in the plasma as an antibody response to trypsin or a trypsin-activated antigen.

Elicitation of elevated antibody titer by trypsin suggests that anaphylaxis may contribute to production of the shocklike component of acute pancreatitis.

Elevated antithrombin titers were observed in 90% of 55 patients who had acute pancreatitis studied by Irving Innerfield, M.D. Titers were not elevated in 150 healthy persons. Less than 3% of 150 ambulatory medical patients and 304 patients with acute abdominal conditions had increased antithrombin levels.

Chronic relapsing pancreatitis in remission is difficult to diagnose and may be confused with primary gastrointestinal or gallbladder disturbance. Diagnosis of chronic pancreatitis in a quiescent stage is greatly facilitated by determining the antithrombin titer one hour after subcutaneous injection of 1 cc. of 1:2,000 Prostigmine and comparing with a fasting control sample obtained before Prostigmine injection. Great increase in antithrombin appears after such cholinergic stimulation in patients who have intrinsic pancreatic disease.

Acute pancreatitis: the antithrombin titer as an aid in diagnosis and prognosis. New York State J. Med. 52:2239-2243, 1952.

Evolutionary development of the shoulder is basis for surgical technic to control external rotation.

Recurrent Dislocation of Shoulder

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Cleveland Clinic, Cleveland

HARRY W. O'DELL, M.D.
Akron Clinic, Akron

SHOULDER joint stability may be enhanced by restoration of the pectoralis minor muscle as an active internal rotator. This concept is a result of studies on the evolutionary development of the shoulder joint in species ranging from the lemur and old world monkey to man (Fig. 1).

The pectoralis minor inserts into the humerus in the human embryo, in evolutionary species, and in 1% of adult human beings. In 99% of adults, the insertion has moved to the coracoid process.

From a theoretic standpoint, humeral insertion of the pectoralis minor should act according to the Sherrington law of reciprocal innervation and show tension in all phases of rotation, thus actively inhibiting external rotation. Any procedure which controls external rotation is successful in therapy of recurrent shoulder dislocation.

A surgical technic based on these principles, which has been used for the past two years with gratifying results in 16 cases of recurrent dislocation of the shoulder, is offered by James A. Dickson, M.D.,

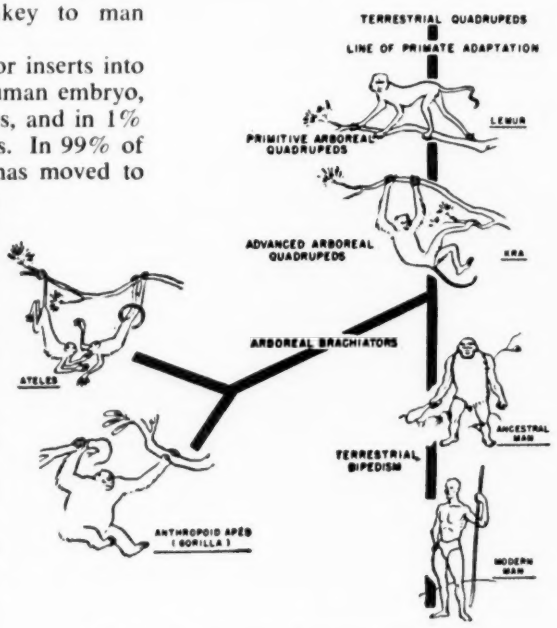


Fig. 1. Phylogenetic development of man

A phylogenetic study of recurrent anterior dislocation of the shoulder joint. Surg., Gynec. & Obst. 95:357-365, 1952.

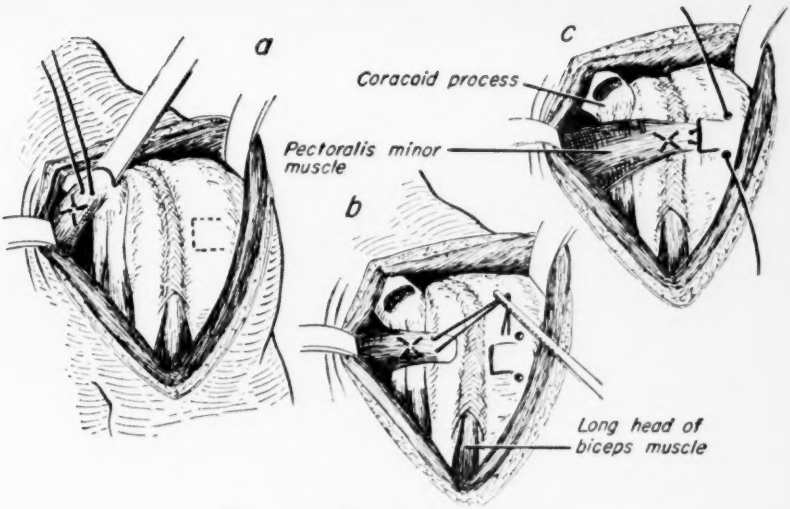


Fig. 2. Details of surgical technic

and Harry W. O'Dell, M.D. The procedure is as follows:

First, a deltopectoral incision is made. A portion of the deltoid may be dissected from the clavicle to facilitate exposure of the humerus. With the deltoid reflected, the pectoralis minor insertion is isolated (Fig. 2*a*). An interlacing silk suture is securely placed in the tendinous portion.

With a small curved chisel, a cortical flap from the coracoid is removed, together with the muscle insertion. The flap should be large enough to preserve all tendinous attachments. If precautions are not observed, the tendon may fray or be placed under strain.

Next a small trap door (Fig. 2*b*) is made on the greater tuberosity just lateral to the bicipital groove. The groove is made over the center of rotation to prevent increased tension in abduction. Two drill holes are made just lateral to the trap door. With the arm in internal rotation, the pectoralis minor is then brought over to the humerus and placed in the trap door by fastening the silk suture securely (Fig. 2*c*). Additional sutures may be added.

The transplanted muscle has approximately the same tension as in the original position. The newly placed pectoralis minor tendon tightens in external rotation but no increase in muscle tension appears in any other position.

Postoperative care consists of fixing the arm to the body for four weeks in a modified Velpeau bandage. Further immobilization is done by a sling. The patient uses exercises to strengthen the internal rotators. Activity is resumed gradually. Complete rehabilitation is established in eight to twelve weeks.

Operations to provide both knee and hip extension will improve walking with cerebral spastic paralysis.

Transplantation of Hamstring Tendons

G. W. N. EGGERS, M.D.
University of Texas, Galveston

TO better the walking gait of patients with cerebral spastic paralysis, knee extension must be increased and hip flexion relieved.

The knee extension is improved by division of the patellar retinacula which permits the quadriceps femoris to act on the tibia.

The hip flexion is relieved by transplanting the tendons of the semimembranosus, semitendinosus, gracilis, and biceps femoris to the respective posteromedial and posterolateral sides of the femoral condyles. The contraction of the hamstrings after transplantation acts to extend the hip and indirectly to retain knee extension (Fig. 1). This force improves the gait because the hamstrings do not flex the tibia at the knee.

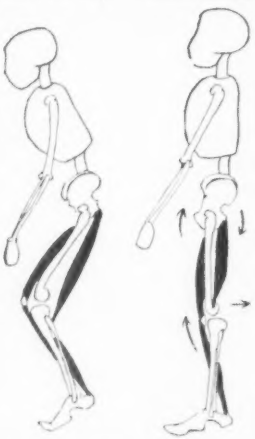


Fig. 1. Effect of hamstring transplant

The popliteus, gastrocnemius, and sartorius muscles prevent knee joint recurvature after hamstring transplantation and must not be displaced because of the danger of interrupting vascular and nerve supplies. If the hamstrings are required for knee support on account of postoperative knee recurvature, a rare contingency, the tendons can always be recovered from the femoral condyles and placed in former positions.

In the technic used by G. W. N. Eggers, M.D., incisions for the hamstring transplants are made on the medial and lateral sides of the knee-joint area with the patient prone. The lateral incision, about 3 in. long, is made over the biceps tendon with ends curved to prevent scar tension. The distal end is curved anteriorly just proximal to the fibula head.

The biceps femoris tendon is isolated, with care taken to preserve the common peroneal nerve, and divided before bifurcation (Fig. 2). The tendon is then placed proximally in the subperiosteal groove on the posterolateral margin of the condyle. Silk sutures are used; sufficient fibrous tissue is present for secure anchorage. The periosteum may be divided in making the sub-

Transplantation of hamstring tendons to femoral condyles in order to improve hip extension and to decrease knee flexion in cerebral spastic paralysis. J. Bone & Joint Surg. 34-A:827-830, 1952.

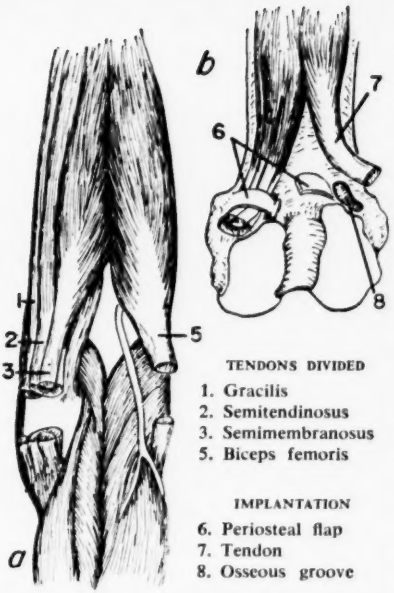


Fig. 2. Division and transplantation of tendons

periosteal tunnel. The medial side of the tendon must rest in the groove, ensuring eventual union with the bony portion of the condyle.

The medial incision is posterior to the sartorius muscle, or may follow the tendons from the medial condyle to the tibial insertion, and has curved ends. The semimembranosus, semitendinosus, and gracilis are divided about ½ in. from the insertions and placed in the subperiosteal groove.

The ends of the divided tendons are sutured to the fibrous tissue on the posteromedial side of the femoral condyle, and the tendons rest on the exposed bone of the subperiosteal tunnel for secure fixation.

The knee joint is immobilized in a cast or splint for three weeks.

If talipes equinus is present, a soleus neurectomy through a lateral incision is the best treatment, with or without heel-cord lengthening. As walking improves after hamstring tendon transplantation, neurectomy and tenoplasty may not be needed, hence are not done immediately.

¶ **PAIN IN PANCREATITIS** is relieved, other symptoms are ameliorated, and recovery apparently is expedited by continuous epidural block. Thomas Walker, M.D., and W. E. Pembleton, M.D., of the Medical College of Virginia, Richmond, ascribe the improvement of 15 consecutive patients so treated to drainage of the pancreatic enzymes into the duodenum brought about by relaxation of the sphincter of Oddi and to dilatation of the spastic blood vessels in the involved area. A plastic catheter is introduced into the epidural space through a Huber tipped needle and left taped in place for as long as several days. Through the tube, 10 cc. of a 1% or 0.5% procaine or xylocaine solution with epinephrine is injected at intervals of from four hours to once daily. Hypotension is an occasional complication but is readily controllable with the use of vasopressors.

Anesthesiology 14:33-37, 1953.

Procedures to maintain blood flow through the venous system are valuable in operative cases.

Thromboembolic Disease after Surgery

ARTHUR W. ALLEN, M.D.
Massachusetts General Hospital, Boston

ROUTINE measures should be instituted for the prevention of venous thrombosis and pulmonary embolism in surgical cases.

Stasis in the deep veins of the legs is an important factor in thromboembolism. Specific therapy to reduce stasis will decrease the incidence of morbidity and fatal embolism, states Arthur W. Allen, M.D.

Preoperative prothrombin time should be recorded for all adults. Legs with large superficial varicosities are bandaged before operation.

Care must be used to eliminate pressure on the leg veins during surgery. The anesthesiologist should maintain adequate oxygenation at all times. During long operative procedures, the patient should be placed in some Trendelenburg position at intervals when feasible.

Trauma to large pelvic veins by retractors or during dissection must be avoided, and any large vein that is sectioned should be interrupted as near the undamaged parent vein as possible.

Procedures should be accomplished as quickly as consistent with the problem at hand. Dressings are lightly applied.

The foot of the bed should be elevated by 8-in. blocks postoperatively until ambulation, unless inadvisable. Elastic bandages or lightweight elastic stockings should be kept on the legs from feet to tibial tubercles. The patient is turned from side to side frequently until awake and is then helped to turn and also encouraged to breathe deeply.

The patient's joints and muscles, with legs elevated, should be passively exercised by the nurse every four hours. Later the patient can perform such exercises. Early walking, but not sitting, is practiced. Regular shoes are worn for walking.

Dicumarol is administered by mouth as soon as feasible postoperatively. Another dose is given forty-eight hours later according to the effect of the first administration on the prothrombin time; reduction of the time below 50% of normal is probably not safe for elderly people.

For aged or very decrepit persons who are unsuited for other measures, prophylactic bilateral superficial vein interruption is done in the legs if prolonged bed rest seems necessary. This procedure should always be used at the time

Management of thromboembolic disease in surgical patients. Surg., Gynec. & Obst. 96:107-114, 1953.

of thigh amputations for arteriosclerotic gangrene.

If a thrombosis has occurred, therapeutic methods depend on the patient's age and general condition and concomitant disorders.

As soon as the diagnosis is established, by lung infarct or leg signs, heparin or Tromexan is given. Dicumarol may be administered at the same time and, after forty-eight hours, a safe level of blood coagulability can be maintained by dicumarol alone.

For elderly persons or patients with large emboli, bilateral venotomy, thrombectomy, and interruption of the femoral veins is done first. Anticoagulants can be added in twenty-four hours. If swelling and pain in the legs persist after anticoagulants or vein ligation, procaine blocks of the lumbar sympathetics are helpful.

When thrombophlebitis is noted during a long period of bed rest in spite of anticoagulant therapy, chances of early and complete recovery are best if femoral vein interruption is done, with subsequent continuation of anticoagulants.

Prothrombin times must be determined routinely when dicumarol is being administered. For outpatients, the time is determined thrice weekly. Anticoagulants should be continued until the danger of fatal embolism is passed, usually about twenty-seven days after the diagnosis of thrombophlebitis is made.

Tracheotomy in Crushing Chest Injuries

B. NOLAND CARTER, M.D., AND JEROME GIUSEFFI, M.D.

NONPENETRATING thoracic injuries may be treated simply and effectively by tracheotomy.

The procedure procures a clear airway, relieves laryngeal obstruction, and reduces the dead space in the respiratory tree, thus allowing more efficient utilization of tidal air. Consequently, the loose thoracic wall becomes stabilized, pain is relieved, and breathing eased, state B. Noland Carter, M.D., and Jerome Giuseffi, M.D., of the University of Cincinnati.

If chest injury is not severe and aeration is adequate, intercostal nerve block is done first. Tracheotomy is used later if cough is inadequate to raise secretions or if respiratory function is jeopardized.

For severe chest trauma, tracheotomy is done immediately and oxygen is administered. Thoracentesis may reveal sufficient air or blood to cause respiratory distress. A small intrathoracic catheter is then inserted and connected to waterseal drainage. When the air leak has ceased, the thoracotomy tube is utilized, as well as suction, to promote rapid expansion of the collapsed lung.

The use of tracheotomy in the treatment of crushing injuries of the chest. Surg., Gynec. & Obst. 96:55-64, 1953.

Preoperative diagnosis of pyloric hypertrophy is often missed, though roentgenograms are usually indicative.

Pyloric Hypertrophy in Adults

WILLIAM P. KLEITSCH, M.D.
Creighton University, Omaha

THE roentgenographic appearance of hypertrophy of the pyloric sphincter in the adult is sufficiently typical to be readily diagnosed by the radiologist or gastroenterologist. Pyloroplasty or subtotal gastrectomy usually relieves the symptoms.

Congenital pyloric hypertrophy is uncommon but not rare in adults, states William P. Kleitsch, M.D. If a Ramstedt pyloroplasty has not been done in childhood, the anomaly will persist.

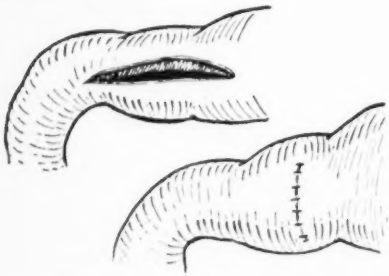


Fig. 1. Pyloric hypertrophy

With uncomplicated hypertrophy the pyloric sphincter is transected longitudinally and the incision closed transversely.

The hypertrophied sphincter can produce symptoms alone or together with associated or secondary lesions. In the uncomplicated cases, epigastric pain occurs, aggravated by the ingestion of food and largely alleviated by vomiting. The pain is not relieved by antacids, and night pains are notably absent.

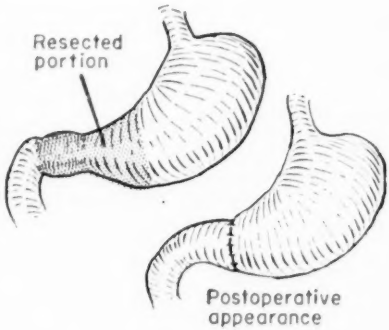


Fig. 2. With muscle thickening

If muscular hypertrophy makes transverse closure awkward, pyloric resection and Billroth I gastrectomy are employed.

A relatively high-grade obstruction may develop, manifested by a postprandial epigastric mass which disappears after vomiting.

The most frequent complication is peptic ulceration in the stomach, the duodenum, or the narrowed pyloric canal. The duodenal ulcer is probably a distinct and separate entity, but the gastric ulceration may well be caused by stagnation of the gastric contents with pro-

Diagnosis and treatment of pyloric hypertrophy in the adult. Arch. Surg. 65:655-664, 1952.

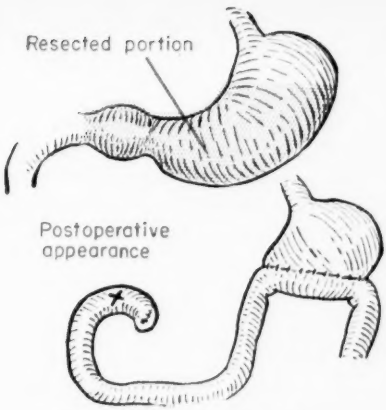


Fig. 3. With duodenal ulcer

High subtotal gastrectomy is advisable if hypertrophy is associated with duodenal ulceration, fibrosis, or stenosis.

longed exposure of the gastric mucosa to digestive juices. Ulcers within the pyloric canal are probably of traumatic origin. When a duodenal or gastric ulcer coexists, the symptoms are indistinguishable from those with stenosing duodenal ulcer.

Roentgenograms of the upper gastrointestinal tract reveal a constant elongated and narrowed pyloric canal, termed the "pyloric string sign," which is not obliterated by antispasmodics. The thickened pyloric sphincter gives the impression of a filling defect surrounding the pyloric antrum.

Since pyloric hypertrophy represents an organic obstruction to the passage of food through the gastrointestinal tract, radical surgery is required. If pyloric hypertrophy is the only lesion, simple longitudinal transection of the sphincter is done, carrying the incision well into the stomach and duodenum, with transverse closure of the resulting defect—Heineke-Mikulicz pyloroplasty (Fig. 1).

If the muscular hypertrophy has so developed that transverse closure of a transection may be awkward because of difficulty in inverting the thickened muscle, complete excision of the pyloric muscle and restoration of the normal continuity by a Billroth I gastrectomy is necessary (Fig. 2).

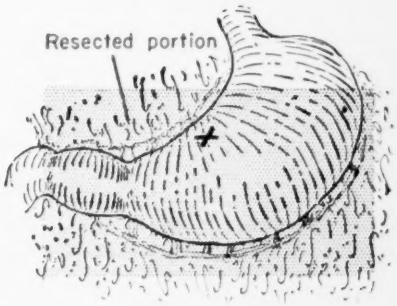


Fig. 4. With gastric ulcer

With stomach ulcer, resection should be en bloc a safe distance above the lesion and should include the regional lymph nodes.

If a duodenal ulcer, duodenal fibrosis, or stenosis is found, subtotal gastrectomy should be done (Fig. 3).

When the ulceration is gastric, subtotal gastrectomy will also be necessary and, because of the possibility of cancer, is performed at a safe distance above the ulcer, including the regional lymph nodes in resection (Fig. 4).

For rapid or continuous intravenous transfusion or fluid therapy, plastic catheters are desirable.

Plastic Intravenous Catheter

DONALD W. SMITH, M.D.
Jackson Memorial Hospital, Miami

R. S. SAPPENFIELD, M.D.
Veterans Administration Hospital, Coral Gables, Fla.

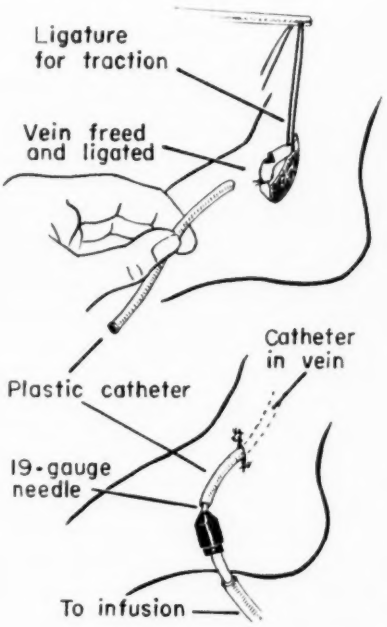
W. J. FINK, M.D.
Veterans Administration Hospital, Fayettesville, Ark.

REPEATED and massive blood transfusions and parenteral fluid replacement are most efficiently and rapidly performed through a plastic intravenous catheter.

Among indications for this type of catheter are postoperative shock, severe anemia requiring preoperative multiple cell suspension transfusions, and internal bleeding after ruptured ectopic pregnancy, esophageal varices, or peptic ulcer. The device is also valuable for maintaining the fluid equilibrium of extremely ill or dehydrated infants and children, especially for exchange transfusions in neonatal hemolytic diseases.

A metal cannula and needle often create local complications during prolonged intravenous infusion, traumatizing the vein and causing thrombosis or perforation with extravasation. With a plastic catheter securely taped to the skin, the limb has full movement and mechanical trauma to the endothelial wall is negligible.

The polyethylene or polyvinyl plastic intravenous catheters of varying length and gauge used by Donald W. Smith, M.D., R. S. Sap-



Surgical insertion of catheter

Use of the plastic intravenous catheter for multiple and massive transfusions and prolonged intravenous fluid therapy. Surg., Gynec. & Obst. 95:775-777, 1952.

penfield, M.D., and W. J. Fink, M.D., are kept sterile in sealed glass tubes containing a 1:1,000 zephiran solution. To use, the glass tubing is alcohol-cleansed and broken and the catheter removed.

The method of insertion depends upon the available veins. A 15-gauge needle attached to a small hypodermic syringe is inserted into a suitable vein. The tourniquet is removed and the extremity is draped by a sterile towel extending under the needle hub. The syringe is detached from the needle and the catheter is then threaded through the 15-gauge needle into the vein for approximately one-half the needle's length. The 15-gauge needle is then withdrawn, counterpressure being used with the fingers over the vein to hold the catheter in place.

The 19-gauge needle on the infusion set is then inserted into the free end of the catheter. The catheter is firmly anchored to the skin with adhesive tape.

When surface veins capable of accommodating a 15-gauge needle are not available, a suitable vein, usually a medial malleolar or antecubital vein, is exposed surgically and the catheter inserted directly (see illustration). This procedure is often necessary for children, obese women, and other patients with small, inaccessible, or collapsed veins.

To close and retain the catheter in place between transfusions when continuous drip is not desired, a small hypodermic syringe containing physiologic saline may be firmly attached to the needle in the catheter. The saline is then injected to expel blood from the catheter and the plunger is secured and taped to the skin. Other methods of temporarily plugging the catheter include attaching a Luer-Lok plug to the needle or removing the needle and sealing the catheter tip by flame. Catheters may be kept in place for two or more weeks.

Vascular irritation is occasionally seen when concentrated solutions, irritating medications, or amino acids are administered through a large catheter into a small vein.

¶ **LEG CRAMPS IN PREGNANCY** are prevented or relieved by limiting the patient's intake of milk and giving from 0.5 to 0.9 gm. of aluminum hydroxide gel with each meal. Ernest W. Page, M.D., and Emery P. Page, M.D., of the University of California, San Francisco, find that ingestion of large quantities of milk or medication with dicalcium phosphate predisposes to muscular tetany by causing a fall in diffusible calcium and a rise in inorganic phosphorus concentrations in the blood. The condition occurs in half the women in private practice between the twenty-fourth and thirty-fourth week of pregnancy; the frequency is much less in semi-indigent gravidas consuming limited amounts of phosphorus-containing proteins.

Obst. & Gynec. 1:94-100, 1953.

When pregnancy goes beyond term, the larger the fetus, the greater the urgency for intervention.

Effects of Prolonged Pregnancy

ANDREW TEMESVARY, M.D.
University of Zurich, Switzerland

CONTINUATION of pregnancy beyond the usual delivery date is a pathologic condition with increasingly grave implications for the fetus. Intervention is sometimes essential.

Although prolonged pregnancy is usually diagnosed arbitrarily as gestation that outlasts the two hundred ninetieth day after the last menstrual period, Andrew Temesvary, M.D., points out that prolonged pregnancy in the biologic sense is quite different from gestation lengthened only in regard to time. Distinction lies in the danger to fetal life implicit in the biologic type of prolongation, which often cannot be demonstrated certainly even after delivery. The antepartum diagnosis is therefore difficult. However unreliable, excessive time of gestation is the only practicable criterion of biologically prolonged pregnancy.

Duration of pregnancy, furthermore, may be inaccurately measured because the woman has had an irregular, shortened, or prolonged cycle, early ovulation, or bleeding during pregnancy.

A study of 16,824 pregnancies in which calculation of the last period was possible revealed that 30.7% lasted two hundred eighty-five days or more from the last menstrual period. Women who have had a prolonged pregnancy are not more likely to have another prolonged gestation than are other women.

The causes of fetal death with a prolonged pregnancy are not known. Although fatality rates are higher when the babies are extremely large or small, the size of the fetus does not alone explain the death. Other possible causes are intrauterine hypoxia associated with aging of the placenta and primary uterine weakness resulting from stretching of the uterus by large babies or hydramnion.

After the normal delivery date, infant mortality increases in an approximately linear curve. Large babies are 3.5 times more likely to die if delivered on the three hundredth day than at term.

Just after the correct delivery date, antepartum death rates are higher than the postpartum; later this situation is reversed. Male death rates from all causes are higher than female, particularly after the onset of labor. Drug induction of labor is associated with higher death rates just after the expected delivery date is passed than later, but in general the mortality

Prolonged pregnancy and its consequences. West. J. Surg. 60:627-635, 1952.

rate is lower when birth is spontaneous, 0.18%, than when induced, 1.52%.

Monstrosity is a factor. Because of the hydramnion causing uterine overdilatation, contractions may be weakened and pregnancy thus prolonged with hydrocephalic and anencephalic fetuses.

Once a diagnosis of prolonged pregnancy has been made—especially if the fetus is large—early intervention is essential. Each of the 3 means available has disadvantages: *Cesarean section* carries increased maternal mortality, but is best for the child. *Drug induction* endangers the fetus. *Mechanical induction* has risk for both mother and child.

Long labor is badly tolerated by the fetus in any case.

Premature Rupture of Membranes

L. A. CALKINS, M.D.

SPONTANEOUS rupture of the amniotic sac before the onset of labor occurs in about 1 of 7 deliveries. Such ruptures increase the chances of premature delivery and of fetal mortality, usually from pneumonia or prolapsed cord.

In addition, the first stage of labor is usually shortened and blood loss in the third stage slightly increased. Maternal morbidity may be greater but maternal mortality is not affected.

L. A. Calkins, M.D., of the University of Kansas, Kansas City, advises hospitalization when membranes rupture spontaneously. Prophylactic penicillin should be given because of the likelihood of fetal infection.

Most gravidas deliver within twenty-four hours of the rupture, and no special management is necessary. Avoidance of upward displacement of the presenting part is recommended. All-out efforts to induce labor are not justified. Cases for induction should be carefully selected. Castor oil induction succeeds in only a few cases; oxytocic drugs, especially by slow intravenous drip, are more effective.

If rupture occurs in the thirty-third or thirty-fourth week, labor should not be induced, since the advantages to be gained by another week or so of pregnancy outweigh the dangers of possible prolapsed cord or intrapartum infection.

Infection not occurring within seventy-two hours after rupture is not likely thereafter. A patient, therefore, who does not have free drainage of fluid or infection seventy-two hours after spontaneous rupture may be sent home to await onset of labor.

Premature spontaneous rupture of the membranes. Am. J. Obst. & Gynec. 64:871-877, 1952.

Definitive diagnosis is basic to successful surgical treatment of female urinary incontinence.

Urinary Incontinence in Women

AXEL INGELMAN-SUNDBERG, M.D.
Karolinska Sjukhuset, Stockholm

CORRECT treatment of urinary incontinence is dependent on an exact diagnosis. The etiology is not uniform and the various causes of incontinence, not including fistulas, may be classified as:

• Mechanical Disturbances of the Sphincter

Insufficiency of pelvic floor—Inadequate pubococcygeal musculature results in stress incontinence. An abnormal descent of the bladder neck occurs. A patient with stress incontinence has symptoms only in the erect posture or when sneezing and coughing. Usually she has borne several children.

Scars impeding internal sphincter function—Urinary incontinence sometimes develops after pelvic surgery, especially for prolapse. The urethral meatus is distorted and unable to close normally because of fixation by scar tissue. Patients with scar incontinence, which is recognizable by urethroscopic examination, have always had pelvic or vaginal surgery performed shortly before onset of symptoms.

Destruction of the internal sphincter—In a few cases of vesicovaginal fistula involving the bladder neck, continence is not achieved even by fistula repair.

Congenital malformations—Urinary incontinence from childhood may be caused by hypoplastic bladder, wide posterior urethra, hypoplastic internal sphincter, or other malformation.

Urethral diverticula or inflammation of the urethral glands or of the posterior urethra—Women with urethral diverticula often have dribbling after micturition and pass urine during coitus. Burning pain is frequent with the condition and with infection of the paraurethral glands or posterior urethritis.

• Neurogenic Lesions

Hypertonic or uncontrolled bladder associated with a neurologic lesion—Lesions include syringomyelia, syphilis, arteriosclerosis.

Nonspastic bladder associated with a neurologic lesion—The only symptom, besides the incontinence, may be lack of sensitivity inside the bladder.

Enuresis nocturia

• Combined Mechanical and Neurologic Disorders

Diagnosis

The examination is of utmost importance. A simple test for stress incontinence is to place an Allis clamp in the anterior vaginal wall

Urinary incontinence in women, excluding fistulas. Acta obst. et gynec. Scandinav. 31:266-291, 1952.

near the bladder neck after local anesthesia of the mucosa. The bladder is filled and, with the patient erect, the forceps is pushed upward and forward. If this prevents leakage during coughing and straining, repair may be successful.

Roentgen examination with a radiopaque fluid filling the bladder is always done. The frontal position demonstrates the shape of the bladder and funneling of the bladder neck. The lateral position is best to show ptosis, urethral shape, and position and distance of bladder neck from symphysis.

Cystoscopic study should be done in all cases. Lack of sensitivity, an early sign of neurogenic bladder, can be determined by touching the cystoscope to the trigone. Patients can normally tell whether the trigone is touched on the left or right or middle.

Urethroscopic examination will reveal diverticula and inflammation of the posterior urethra.

The water pressure necessary to open the sphincter should be determined to evaluate the sphincter function.

THERAPY

Conservative methods—Methylscopolamine is of value in cases of urgency, especially those of neurogenic origin. Tidal drainage is also useful. With flaccid bladders, antihistamine drugs may give relief.

Operative methods—Repositioning of the bladder neck behind the symphysis is the chief object of surgery for incontinence. Axel Ingelman-Sundberg, M.D., in addition to the usual vaginal repair, divides the pubovesical ligament and thereby prevents distortion of the internal sphincter, a source of failure with many operations. The results of the operation are excellent for stress incontinence with pathologic ptosis of the bladder neck.

The urethra-kinking operation, extending the urethra by forming a mucous membrane, muscle-enclosed tube, is used in cases of fixation of the urethral sphincter from scar tissue or congenital hypoplasia or destruction of the sphincter and for patients with nonspastic bladders associated with neurologic lesions or enuresis.

¶ ECTOPIC PREGNANCY is twice as frequent since the introduction of penicillin therapy. Use of the drug may favor tubal pregnancy by preventing occlusion or reestablishing patency of a tube after the development of irreversible structural changes in the endosalpinx. Leon Krohn, M.D., M. S. Priver, M.D., and M. H. Gotlib, M.D., of Los Angeles find the incidence in their private practice to be 4 times as great as ten years ago and 3 times greater than in women treated by other physicians at Cedars of Lebanon Hospital. This difference in incidence ratio appears to be directly related to the number of patients who receive penicillin therapy for pelvic infections.

J.A.M.A. 150:1291-1292, 1952.

The death rate with cancer of the vagina is shockingly high; improvement in therapy may be possible.

Primary Carcinoma of the Vagina

IRWIN H. KAISER, M.D.
University of Minnesota, Minneapolis

AMONG cancers of the female genital organs producing early signs and symptoms, primary carcinoma of the vagina yields by far the lowest five-year cure rate, approximately 15%. Fortunately the neoplasm is one that is comparatively uncommon.

Evaluation of therapeutic measures is difficult because cases are not often seen in significant numbers. However, the best treatment is irradiation, finds Irwin H. Kaiser, M.D., who describes results in treatment of 55 women at the University of Minnesota between 1927 and 1950.

Surgery to date has contributed little to the successful management of this cancer. Bold application of the resources of irradiation and surgery constitutes the main hope for improvement of the present five-year cure rate.

Greatest tumor destruction probably results from the administration to the tumor of adequate doses of irradiation, within the limits of tolerance of the adjacent normal viscera, in the shortest possible time. But maximum daily doses of deep roentgen rays, 300 to 400 r in air to each field, are already being administered. Therefore, further increase seems out of the question. Prolongation of therapy, however, may be feasible and, in this way, total dosage of deep roentgen rays could be increased to 5,000 tissue r.

More important is an increase in radium treatment, for cure of the local lesion is induced primarily by short focal distance therapy. Neglect to cure the local lesion is responsible for most of the failures in vaginal cancer. The radium dosage could be increased to 10,000 gamma roentgens without varying the present time factor.

The control of vaginal cancer with distant metastases, especially to the inguinal lymph nodes, is probably primarily surgical. The basic operation must include hysterectomy, vaginectomy, pelvic lymphadenectomy, vulvectomy, and inguinal lymphadenectomy. In appropriate cases, resection of the bladder or rectum, or both, may be necessary.

Such surgical therapy is very radical and carries a high primary mortality, but these patients have heretofore been doomed.

Behind any hope for salvage with irradiation or surgery stands early diagnosis. Physicians must be alert to recognize this disease. Symptoms are usually produced by

Primary carcinoma of the vagina. Cancer 5:1146-1160, 1952.

sloughing or bleeding from the tumor, rarely by a mass or by involvement of other organs. The chief symptoms are vaginal bleeding or discharge. The incidence increases with advancing age, being highest in the age group from 60 to 69. The cancer may be found as early as the third decade, however.

The location of the primary lesion in the vagina is important in determining method of therapy and ultimate prognosis. If the cancer is in the upper third of the vagina only, spread to the inguinal nodes has probably not occurred. If the tumor is primarily in the lower two-thirds of the vagina, inguinal nodes may be involved. Posterior wall tumors are primarily in the upper third; anterior wall tumors, chiefly in the lower two-thirds of the vagina.

Premalignant Phase of Endometrial Cancer

HAROLD SPEERT, M.D.

UNEXPLAINED abnormal proliferative patterns in the postmenopausal endometrium demand close observation and may even justify hysterectomy as a prophylactic measure. Atypical hyperplasia of the endometrium in the postmenopausal uterus, in the absence of estrogenic therapy or a feminizing ovarian tumor, is usually associated with adenocarcinoma, existent or in prospect.

A study of 16 cases of endometrial carcinoma in which curettage was performed at various times before the cancer diagnosis was made is reported by Harold Speert, M.D., of Columbia University, New York City. In 3 of the cases cancer had appeared in the original curettings but was misdiagnosed. In 2 cases normal proliferative endometrium was revealed, but the curettages were made over nineteen years before the discovery of cancer. The remaining 11 cases showed varying degrees of atypical or adenomatous hyperplasia of the endometrium. These curettages were made one to eighteen years before the diagnosis of cancer.

The hyperplasia is characterized by various combinations of epithelial budding, tuft formations within the gland lumens, outpouchings of the gland walls, crowding of the glands, stratification of the epithelium, and pallor of the stained cells. Similar benign endometrial changes may be produced by prolonged estrogen stimulation, therapeutically or from granulosa-theca-cell tumors of the ovary.

The age of the patient merits consideration in an appraisal of endometrial changes. Significance during the menstrual era is uncertain.

The premalignant phase of endometrial carcinoma. Cancer 5:927-944, 1952.

The bizarre signs and symptoms of disseminated lupus erythematosus may lead to erroneous diagnosis.

Disseminated Lupus Erythematosus

MARTIN A. SHEARN, M.D.
Stanford University, San Francisco

BERNARD PIROFSKY, M.D.
New York University, New York City

SYMPTOMS of disseminated lupus erythematosus are many and varied. This collagen disease may involve one or several organ systems, but is essentially a febrile disease of unknown etiology comprising skin lesions, polyserositis, depression of bone marrow elements, and widespread visceral involvement.

The disease has a predilection for females and is usually fatal within less than five years. Among 34 patients, 31 were females, 8 of whom were either above or below the childbearing age.

The most consistent abnormality revealed by laboratory tests in cases of acute disseminated lupus erythematosus, aside from the elevated sedimentation rate, which is nonspecific, is the L.E. cell. Martin A. Shearn, M.D., and Bernard Pirofsky, M.D., found L.E. cells in 29 of 31 patients examined, showing that the technic for identification of the L.E. cell is a highly sensitive and specific indication of the acute disease.

Skin biopsies performed for 13 patients with cutaneous lesions showed changes compatible with disseminated lupus erythematosus in all. Results of biopsy studies of 2 patients without skin lesions were negative.

Anemia is almost invariable with the disease and is usually normocytic and normochromic. Leukopenia and proteinemia are often noted and the albumin and globulin ratio is frequently abnormal.

The bizarre signs and symptoms of disseminated lupus erythematosus often lead to erroneous diagnoses. When the typical skin rash does not appear, the symptomatology may suggest rheumatic fever, rheumatoid arthritis, chronic glomerulonephritis, subacute bacterial endocarditis, thrombocytopenic purpura, sarcoidosis, fever of unknown etiology, or blood dyscrasia of unknown type.

Cardiac symptoms are usually prominent. Systolic murmurs are common and electrocardiographic studies reveal alterations in most cases.

ACTH or cortisone is the best treatment for disseminated lupus erythematosus and usually gives symptomatic relief. Fever, joint symptoms, cutaneous lesions, and serous effusions usually subside ini-

Disseminated lupus erythematosus. Arch. Int. Med. 90:790-807, 1952.

tially. The therapy promotes a feeling of well-being, improved appetite, and weight gain. Despite symptomatic relief, abnormal laboratory findings usually persist.

ACTH or cortisone was given to 20 of 34 patients. Results were encouraging in 14 cases and fair to poor in the others. Severe toxic effects of the hormones are rarely encountered. In addition to hormones, antibiotics are employed extensively, being of special value because poor healing of intercurrent infections is common.

Transfusion reactions are unusually high for patients with lupus erythematosus. Signs of reaction may develop in over one-third of the patients transfused.

No consistent predisposing factor has been found for lupus erythematosus, though a preceding exposure to sunlight or ultraviolet ray is frequent. Because the systemic manifestations precede the cutaneous in 41% of cases, a consciousness of this disease on the examiner's part is essential to correct early diagnosis.

Misdiagnosis of Nevi

MARTIN SWERDLOW, M.D.

PIGMENTED moles are frequently confused with other skin conditions. Of 551 lesions, all clinically diagnosed as nevi, only 61% proved to be such microscopically, according to a study by Martin Swerdlow, M.D., of Michael Reese Hospital, Chicago. Conversely, of 454 lesions found pathologically to be nevi, the clinical diagnosis had been correct in only 74%.

The conditions most often incorrectly called nevi are seborrheic keratosis, squamous-cell papilloma, pigmented neurofibroma, basal-cell carcinoma, and various types of hemangioma. Melanoma was found in 6 of the 551 cases clinically diagnosed as nevi.

The most common misdiagnoses that are made of nevi are papilloma, verruca vulgaris, and melanoma.

Some physicians believe that dermal nevi always remain benign and therefore may be treated superficially. But an appreciable number of benign nevi have a junctional component that is thought by many to be the site of developing malignant melanoma. Many melanomas are said to have been stimulated from preexisting moles by patient or physician. The whole nevus should be removed. Partial removal by caustics, radium, x-rays, or incomplete excision is dangerous.

On the other hand, treatment of many of the lesions confused with nevi need be much less radical than is employed.

Nevi: a problem of misdiagnosis. Am. J. Clin. Path. 22:1054-1060, 1952.

Detriment may be greater than benefit if ophthalmic ointments are misapplied.

Use and Abuse of Ointments

HORACE B. DOZIER, M.D., AND PAUL W. RENKEN, M.D.
Tulane University, New Orleans

WHEN employed properly, ointments are indispensable for local administration of drugs to the eye and eyeball. For instance, great benefit is derived in acute conjunctivitis when drops are used during the day and an ointment is worked into the cul-de-sac just before the patient goes to bed.

Ointments are also valuable for chronic conjunctivitis, blepharitis, styes, chalazia, or pediculosis ciliaris or when combined with massage to overcome slight ectropion of the lower lid and to reduce contracture of scar formation of the skin of the lids.

But ointments should not be applied when the entire thickness of the corneal epithelium is broken or interrupted by a deep ulceration or other lesion. The corneal epithelium has great ability to regenerate and fill in defects caused by trauma, burns, toxic agents, or instrumentation and will recover more rapidly if no agent is used whether in solution, powder, or ointment form.

Tiny globules of ointment may get under the epithelium in any abrasion and mechanically delay healing. U.S.P. lanolin or petrolatum may inhibit restoration of minute corneal wounds; when these medicaments contain anesthetics or sulfonamides, epithelial regeneration is especially retarded.

Ointments should not be used in the following conditions:

Abrasions and lacerations of the cornea

Abrasions caused by and resulting from the removal of corneal foreign bodies

Burns involving the corneal epithelium

Ulcers of the cornea

Any operative procedure that interrupts the corneal epithelium, especially intraocular surgery.

Though penicillin is an exception to the tendency of drugs in ointments to inhibit regeneration and is more effective in ointment form than in solution, sensitivity to this drug so often develops. Because edema of the eyelids, chemosis and folliculosis of the conjunctiva, and brawny tender skin may result, use of penicillin ointment has been discontinued by Horace B. Dozier, M.D., and Paul W. Renken, M.D.

An unused tube of ophthalmic ointment is usually sterile but, once the tube is opened, the ointment is subject to contamination. Infection

The use and abuse of ophthalmic ointments. South. M. J. 45:1071-1074, 1952.

may thus be superimposed upon the regeneration-delaying action of the medication and healing be further retarded.

The active ingredient in an ointment is largely in the form of crystals. The sharp edges of these solids mechanically abrade the cornea and may be responsible for the development of ulcer.

An anesthetic ointment should rarely be used by the physician and never given to the patient for self-medication. The severe pain caused by corneal abrasion, removal of a foreign body, or scrubbing of the cornea with tincture of iodine can best be relieved by bandaging the eye and giving the patient a sedative and a drug for the relief of pain.

When an anesthetic is applied, a bandage is often considered unnecessary. Yet the insensitive and unprotected cornea is then especially liable to injury; winking being diminished, exposure keratitis may result. Healing is speeded by bandaging, possibly because the temperature of the conjunctival sac is raised.

Drops are as effective as an ointment to produce miosis or cycloplegia. Undesirable systemic toxic effects of atropine are more easily controlled when local application is in drop than in ointment form. Fatal poisoning of a child has been reported from use of an ointment containing atropine.

Nausea, vomiting, and abdominal distress associated with excessive use of eserine and Prostigmin are less likely to occur or are better controlled if these substances are given in drops rather than in ointment. Local effectiveness is not decreased.

Tilted Handpiece for Crutch

HERBERT W. PARK, M.D., ELEANORE W. MALONE, R.P.T., AND RUTH STEGLICH, O.T.R.

THE conventional straight handpiece on a crutch is less suitable for the natural grip than is a slightly tilted bar.

A free rod grasped firmly generally assumes an angle of 20 to 25°, which may vary with right and left arm. The crutch should be altered to meet individual needs.

Now employed at the Woodrow Wilson Rehabilitation Center, Fishersville, Va., the new plan improves weight-bearing alignment through the wrist. Crutches are more comfortable and more readily used, comment Herbert W. Park, M.D., Eleanore W. Malone, R.P.T., and Ruth Steglich, O.T.R. Fatigue, blistering, and crutch palsy are reduced.

The tilted crutch handpiece. Arch. Phys. Med. 33:731-733, 1952.

SPECIAL EXHIBIT

MODERN MEDICINE presents an adaptation of the exhibit at the American Medical Association meeting in Denver prepared by Charles A. Janeway, M.D., Children's Hospital, Boston, and H. D. Piersma, Lederle Laboratories, Pearl River, N. Y.

IMMUNE SERUM GLOBULIN (Human)

16% Gamma Globulin

Data, except where otherwise indicated, have been provided through the courtesy of Charles A. Janeway, M.D., and Miss Julia C. Sullivan, from published work and unpublished reports to the Commission on Plasma Fractionation and Related Processes. Edwin F. Voigt, Director of Scientific Exhibits, Lederle Laboratories Division, American Cyanamid Company, New York City. Original artwork by William E. Lovingen, New York City.

IMMUNE SERUM GLOBULIN

LICENSED INDICATIONS FOR USE

1 Modification of measles. The usual complications of measles — bronchopneumonia, otitis media, cervical adenitis, and the like—are believed less likely to ensue if measles occurs in a mild or "modified" form.

2 Prevention and attenuation of infectious hepatitis in circumstances where infection is likely or when exposure is known to have occured. Immune Serum Globulin is thought to give approximately a 6- to 8-week period of passive immunity.

3 Prevention of measles. Under certain conditions, as in severely debilitated children or in institutionalized children with tuberculosis or other similar illness, it is usually advisable to attempt complete protection against measles. Immune Serum Globulin (Human) should be given immediately after exposure to measles.

ADMINISTRATION

Immune Serum Globulin (Human) should not be used for intravenous injection but may be used either subcutaneously or intramuscularly.

PURIFICATION PROCESS

Placental blood is equally as good as blood drawn by venesection as a source of human antibodies. The table below gives a comparison of antibody levels in Gamma Globulins prepared from placental and venous blood, expressed as ratios to reference standard. The steps in preparation and purification of Gamma Globulin are outlined in the table to the right and on the facing page.

Placentas Frozen
after delivery in hospital
Transported by
Refrigerated Truck to
Processing Laboratory
Placentas thawed, ground, and extracted
Purified by
Alcohol Fractionation
Pure fraction of
Gamma Globulin
reconstituted to 16% concentration
Frozen and dried
Clarified and Sterile Filtered
Tested by
Processing Laboratory
and the Commission on Plasma Fractionation and Related Processes, Boston

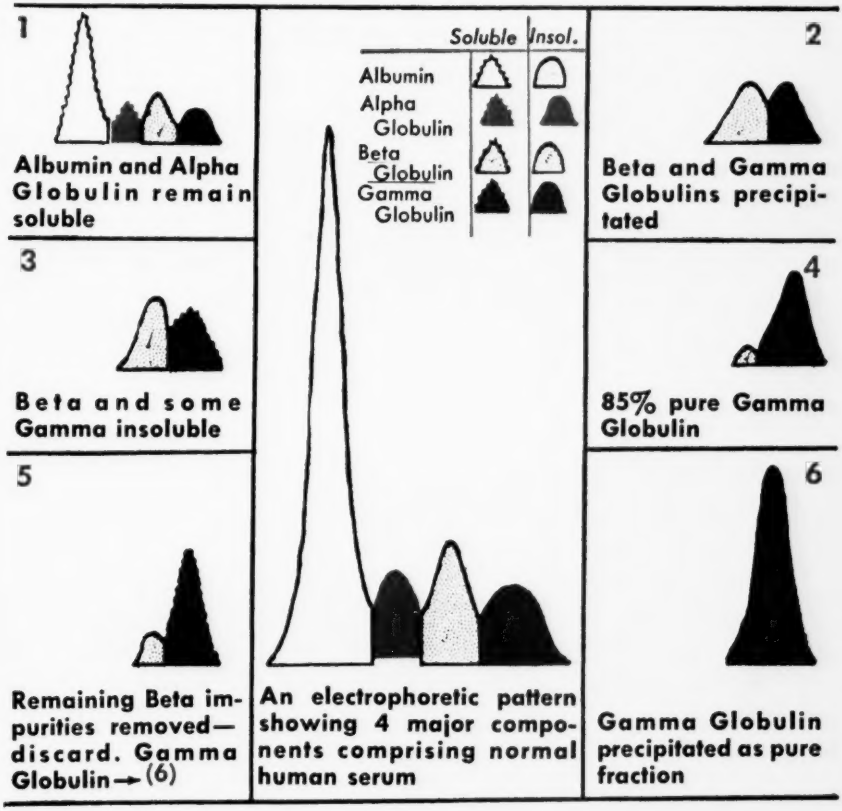
Permission for release obtained from the National Institutes of Health Biologics Control Laboratory, Bethesda, Md.

GAMMA GLOBULINS FROM

	Placental Blood (10 preps.)		*Venous Blood (16)*	
	Average	*Range*	*Average*	*Range*
Typhoid H Agglutinin	0.4	0.4 to 0.5	2.0	0.7 to 4.0
Diphtheria Antitoxin	1.1	0.9 to 1.2	1.7	0.7 to 4.0
Influenza A Neutralization	1.7	0.9 to 3.4	0.9	0.5 to 1.3
Lansing Polio Neutralization	1.2	0.5 to 2.0	0.8	0.2 to 2.0

ALCOHOL FRACTIONATION The fractionation, by alcohol method, of proteins is based on the specific solubility of each protein and is dependent on 5 factors which, when balanced to meet a protein's solubility requirement, will result in that protein's being rendered either soluble or insoluble.

The 5 factors are
1 Temperature
2 Alcohol Concentration
3 pH
4 Salt Concentration
5 Protein Concentration



THE PATTERNS show the 5 steps used to obtain pure Gamma Globulin and the electrophoretic composition at each step

Compiled by Frank H. Clarke, Lederle Laboratories Division, American Cyanamid Co., Pearl River, N.Y.

REPRESENTATIVE ANTIBODIES IN NORMAL SERUM GAMMA GLOBULIN

Gamma Globulin is concentrated 25-fold over normal plasma

Infection	*Antibody*	*Average Titer*	*Approx. Concentration over Normal Plasma*
Typhoid	"H" Agglutinin	94	20
	"C" Agglutinin	10	2
Influenza A	Hirst Test (Homoglutinin inhibitor)	308	10
	Complement-fixing	280	20
	Neutralizing (Mouse)	130	23
Mumps	Complement-fixing	98	20
Diphtheria	Antitoxin	2.6 (units–ml.)	25
Scarlet Fever	Erythrogenic Antitoxin	40 (units–ml.)	22
B-Streptococcus	Antistreptolysin O	2,500 (units–ml.)	25

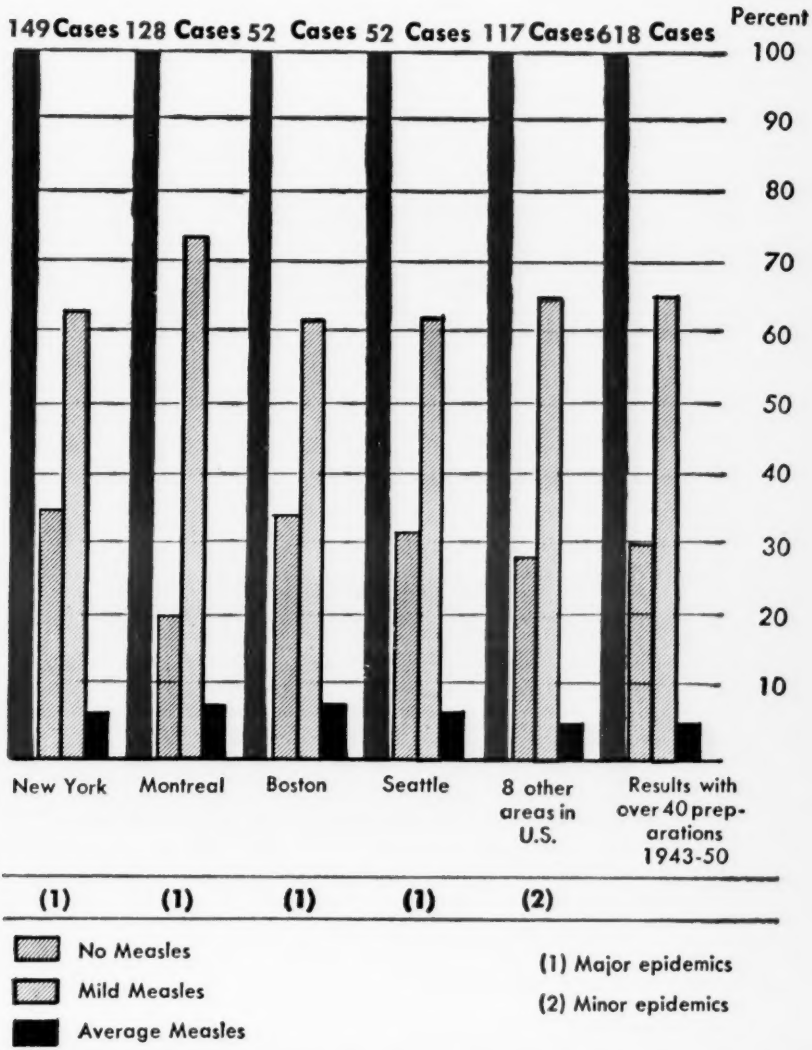
GEOGRAPHIC DIFFERENCES IN IMMUNITY

Geographic differences in immunity and disease experience may affect antibody titers of Gamma Globulin

Gamma Globulin from Blood Donated during 1942-44 in	*Diphtheria Antitoxin Titer (ratio to Ref. Standard)*	*Average Annual Case Rate Diphtheria per 100,000 population (1941-43)*
Pacific Coast Region	0.7	12.5
Eastern States	0.9	3.0
Southwestern States	1.5	27.7
TITER IMPROVED BY ACTIVE IMMUNIZATION		
Professional Donors	3.1	Subjected to Active Immunization Studies

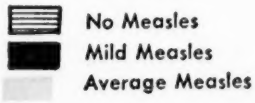
CONSTANCY OF RESULTS IN MODIFICATION OF MEASLES

One preparation of Gamma Globulin (S104) used in different geographic areas in 1950

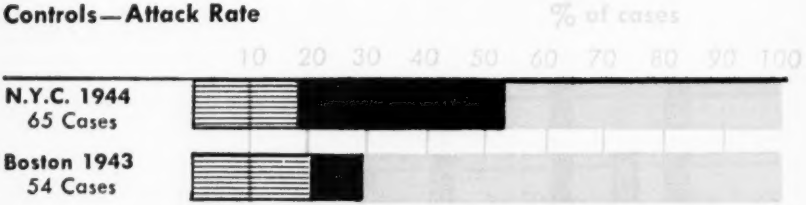


PREVENTION OF MEASLES

Summary of the results with Gamma Globulin in the prophylaxis of measles. Note the correspondence between the size of the dose and the results in intimately exposed children between 6 months and 12 years of age. This analysis has led to a recommended dosage: 0.1 cc./lb. for prevention; 0.02 cc./lb. for modification.

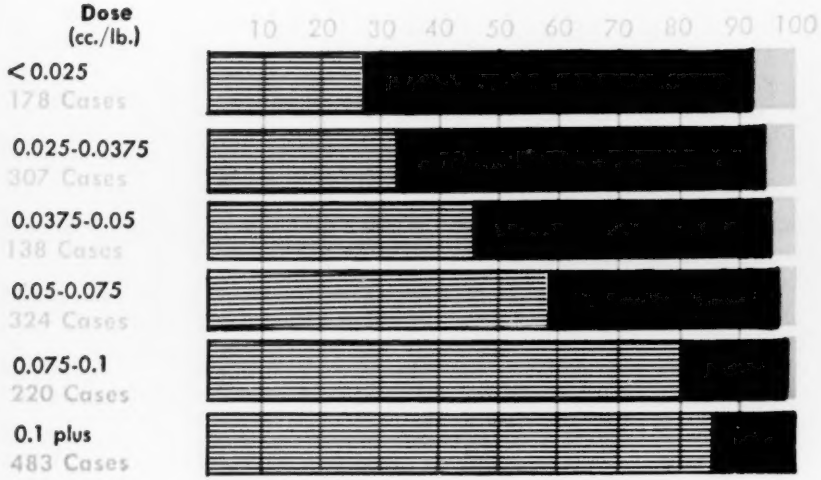


Controls—Attack Rate



CLINICAL EXPERIENCE 1943-46

Children 6 months to 12 years. Intimate exposure. Globulin administered within eight days of exposure. Total number of cases: 1,650.



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USE OF GAMMA GLOBULIN TO CONTROL MEASLES

Gamma Globulin has been used to control measles on pediatric wards. The following practice has been observed: Isolation of the primary case after diagnosis, continued operation of the ward without other measures than isolation of children with mild measles and administration of Gamma Globulin to susceptible children exposed to secondary cases. The dose has been 0.1.cc./lb. The results are tabulated below.

	Outbreaks	*Children*	*Not Followed*	*No Measles*	*Mild Measles*	*Average Measles*
Number	39	395	95	286	13	1
Per Cent				95.3	4.3	0.4

SAFETY Reactions to Gamma Globulin Injection

Total Number of Injections Studied • 2,738

Local • 17	Febrile • 12	General • 6	Total Reactions • 35	Per Cent • 1.2

Homologous Serum Jaundice has not been observed following Gamma Globulin. Only 1 case of hepatitis was observed among a total of 1,977 injections. The same preparation given the child who subsequently had hepatitis had been given to 72 other children, without development of hepatitis. The case occurred during epidemic prevalence of infectious hepatitis in the community and the source of infection is not proved.

HEPATITIS PROPHYLAXIS

The results with Gamma Globulin in the prophylaxis of infectious hepatitis in exposed individuals in 3 separate outbreaks is summarized in the following chart.

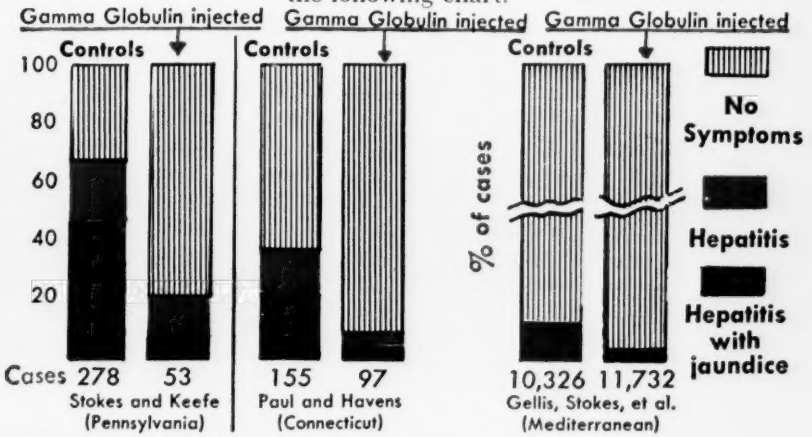

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TABLE OF DOSAGES OF IMMUNE SERUM GLOBULIN (Human)

for MODIFICATION or PREVENTION of MEASLES

Patient's Weight	Dosage for Modification	Dosage for Prevention
15 lb.	0.30 cc.	1.50 cc.
20	0.40	2.00
25	0.50	2.50
30	0.60	3.00
35	0.70	3.50
40	0.80	4.00
45	0.90	4.50
50	1.00	5.00
60	1.20	6.00
70	1.40	7.00
80	1.60	8.00
90	1.80	9.00
100	2.00	10.00
125	2.50	12.50
150	3.00	15.00

for PREVENTION or ATTENUATION of INFECTIOUS HEPATITIS

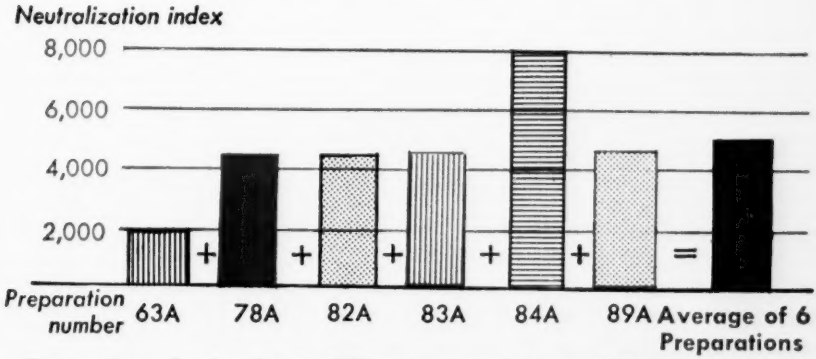
Patient's Weight	Minimum Dose	Maximum Dose
50 lb.	0.5 cc.	3.0 cc.
60	0.6	3.6
70	0.7	4.2
80	0.8	4.8
90	0.9	5.4
100	1.0	6.0
110	1.1	6.6
120	1.2	7.2
130	1.3	7.8
140	1.4	8.4
150	1.5	9.0
160	1.6	9.6
170	1.7	10.2
180	1.8	10.8
190	1.9	11.4
200	2.0	12.0

Except in pregnant or debilitated patients, or among hospital or military personnel, the upper dosage levels should not be used, the aim usually being to obtain active immunity by means of a modified attack of the disease.

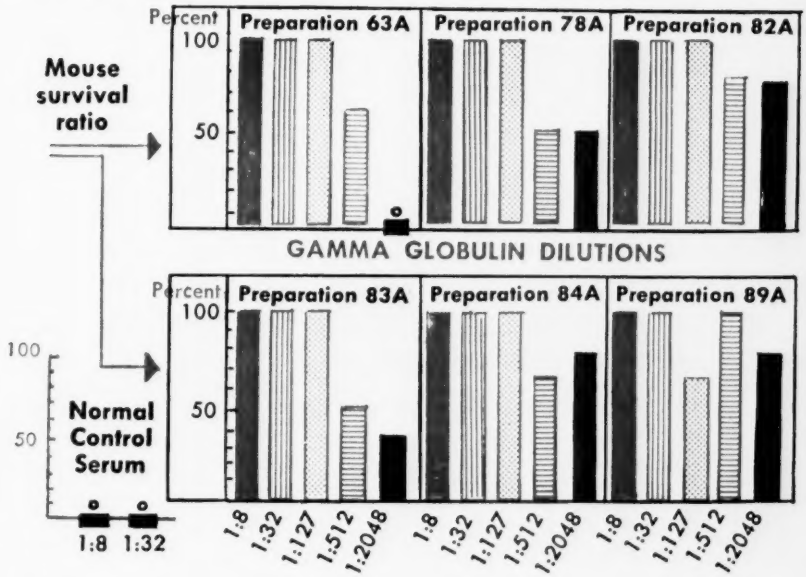
POLIOMYELITIS STUDY

Laboratory Data

Neutralization indices of 6 preparations of Gamma Globulin against Lansing type strain of poliomyelitis virus



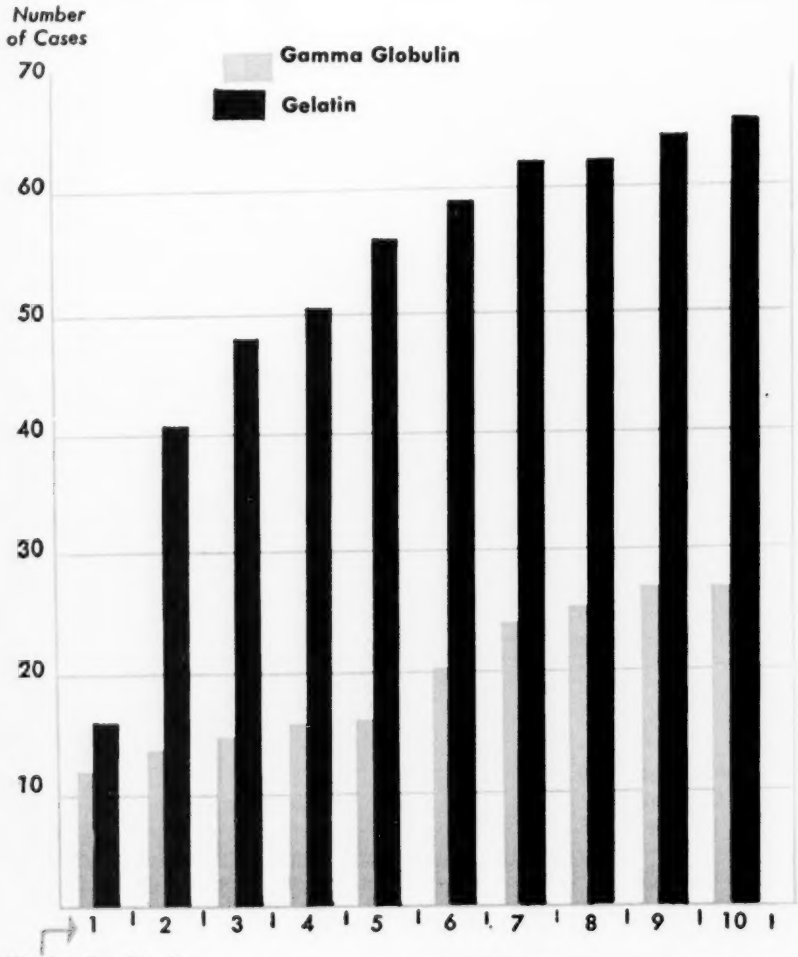
Protection of mice by 6 different preparations of Gamma Globulin against 6 lethal doses of a Lansing type poliomyelitis virus



Charts compiled from data obtained by Victor J. Cabasso, Sc.D., Section of Viral and Rickettsial Research, Lederle Laboratories, American Cyanamid Co., Pearl River, N. Y.

POLIOMYELITIS STUDY

Paralytic poliomyelitis occurring in patients treated with Gamma Globulin in comparison with patients given gelatin is charted below. The cumulative number of cases among children in the Gamma Globulin-treated group and in the control group are compared by weeks after injection.



Reproduced from Hammon et al. J.A.M.A. 150:759, 1952.

POLIOMYELITIS STUDY

SUMMARY

More than 50,000 children, aged 1 to 11, in 3 widely separated epidemic areas composed the group studied for the prophylactic effect of Gamma Globulin against poliomyelitis. Half the children were given a solution of gelatin; the others received Red Cross Gamma Globulin. At the time of injections no one on the inoculating team could identify the solutions or know which the individual child received.

The solutions were given in a single dose into the right buttock in the following dosage:

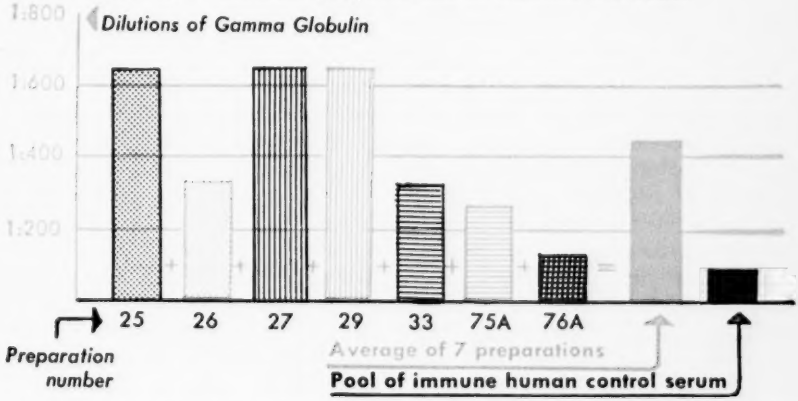
Children weighing up to 35 lb.	4 cc.
Children weighing 35 to 62 lb.	7
Children weighing over 62 lb.	11

Analysis of poliomyelitis occurring in the study groups indicates that the Gamma Globulin injected conferred significant protection. During the first week after injection, severity of paralysis was modified. From the second through the fifth week, there was a high degree of protection; the amount of protection decreased after that time. Further studies may give information about the effect of Gamma Globulin on subclinical infection and the subsequent development of active immunity.

Reproduced from Hammon et al. J.A.M.A. 150:760, 1952.

MUMPS VIRUS

Neutralization of 1,000 minimal infective doses of mumps virus in the chick embryo by 7 different preparations of Gamma Globulin.



Charts compiled from data obtained by Victor J. Cabasso, Sc.D., Section of Viral and Rickettsial Research, Lederle Laboratories, American Cyanamid Co., Pearl River, N. Y.

Combined surgical and endocrine measures are employed empirically in treatment of cancer of the prostate.

Treatment of Prostatic Cancer

HERBERT BRENDLER, M.D.
New York University, New York City

PATIENTS with cancer limited to the prostate should receive the combined benefit of radical perineal prostatectomy and endocrine therapy. The patient with advanced disease, whether or not associated with metastases, is best treated by surgical relief of urinary obstruction and hormonal dosage.

With life expectancy improving, states Herbert Brendler, M.D., the number of men likely to have prostatic cancer is steadily increasing.

Early diagnosis is difficult. The disease is insidious, causing few symptoms until late in the course. By the time of first examination in 90 to 95% of cases, the malignant process is too advanced for curative measures. Most cases deemed potentially curable by radical surgery are asymptomatic preoperatively, being discovered by routine rectal examination.

Prostatic cancer is classified as early or advanced. Early cancer is limited to the prostate gland as shown by rectal examination, has no bone metastases revealed on roentgenograms, and serum acid phosphatase is normal. In contrast, advanced cancer has spread beyond the gland and has bone metastases and elevated serum acid phosphatase.

Early prostatic cancer—Radical perineal excision of the prostate, seminal vesicles, and adjacent bladder neck should be done when cancer is confined to the prostate. The fascial planes along which the cancer spreads should be included in the excision. Although perineural lymphatic infiltration occurs early, distant lymphatic invasion is a late phenomenon.

Applicability of a radical operation is, unfortunately, low. The operative mortality is about 3%. Impotence follows radical prostatectomy in almost all cases.

Occult prostatic cancer—The treatment for carcinoma discovered in a gland removed for apparently benign enlargement is disputed. Some advise radical perineal prostatectomy, others use transurethral resection. Until additional data are available, the radical procedure seems more logical.

Advanced prostatic cancer—Cure is not sought for patients with cancer that has spread beyond the boundaries of the gland, but the aim of therapy is [1] relief of urinary symptoms and [2] endocrine control of the tumor.

Transurethral resection is the most widely employed surgical method for treating bladder neck

Evaluation of current treatment of prostatic cancer. J. Urol. 68:734-743, 1952.

obstructions and is usually very satisfactory. Occasionally, multiple resections are required to cope with continued growth of the tumor.

A small number of patients have severe irritability of the bladder and posterior urethra after transurethral resection and are best treated by permanent suprapubic cystostomy. Open perineal or suprapubic resection is used in some cases of large advanced cancer, obviating the need for repeated operations.

Endocrine measures alone are effective in some instances in relieving the obstructive symptoms. An additional small number of patients have such favorable effects from endocrine therapy with respect to prostatic size, induration, and degree of fixation that radical prostatectomy can be accomplished.

The palliative treatment of inoperable prostatic cancer by androgen control is a milestone. The control of androgens may be brought about by castration or administration of diethylstilbestrol. The combination of both methods seems to be most effective in the nonmetastatic group. In patients with metastases, castration alone is as effective as combined therapy.

Despite the initial improvement with endocrine therapy, recurrence or reactivation occurs. Increasing the dosage to 1,000 mg. daily may be of symptomatic benefit. Changing to another estrogen is helpful. Bilateral adrenalectomy, pituitary radiation, or hypophysectomy has been used for recurrence.

Some patients actually benefit subjectively from testosterone, although many have prompt and severe relapse. Similar effects are reported for progesterone. The intraprostatic injection of radioactive gold seems promising.

Protection from Cancer of the Prostate

ROGER BAKER, M.D.

NEARLY a fourth of men dying after the age of 50 years have unrecognized small cancers of the prostate.

Growth of prostatic cancer is hastened by androgen and retarded by either withdrawal of androgen or administration of estrogen. To avoid activation of an unsuspected tumor, testosterone should not be given to patients past middle life.

At the University of Chicago, Roger Baker, M.D., induced healing in 3 advanced cases with 0.25 to 0.5 mg. of diethylstilbestrol per day. Estrogen was neutralized and symptoms reactivated by 10 mg. of testosterone propionate daily. Much smaller doses may destroy the delicate estrogen-androgen balance in serum and accelerate unnoticed malignant growth.

Studies on cancer prevention in urology. Ann. Surg. 137:29-34, 1953.

Urograms made during an acute attack are necessary for diagnosis in some types of hydronephrosis.

Hydronephrosis in General Practice

REED M. NESBIT, M.D.
University of Michigan, Ann Arbor

THE clinician is well advised to resort to pyelographic examination when a patient describes dyspepsia yet the gastrointestinal roentgenograms are normal. Hydronephrosis may be found, explains Reed M. Nesbit, M.D.

Hydronephrosis is occasioned by obstruction in the urinary passages. The accumulation of urine distends the pelvis of the kidney, causing atrophy of the renal parenchyma.

When the obstruction occurs abruptly and the flow of urine is completely blocked, sudden and intense pain ensues in the kidney and persists until flow of urine down the ureter is reestablished.

Renal colic from calculus blockage is an example of this situation. The pain can be relieved by passing a ureteral catheter beyond the obstruction.

Another familiar example of acute ureteral obstruction is intermittent hydronephrosis, which occurs when the upper ureter is compressed by an anomalous blood vessel or an abnormally located band of fascia. Obstruction is precipitated by displacement of a movable kidney, causing kinking of the ureter where crossed by the vessel or fascia. Certain activities precipitate intermittent hydronephrosis. Thus attacks may be induced by riding in an automobile or by stepping or jumping down.

Lying on the back or on either side occasionally causes pain from hydronephrosis as may ingestion of large quantities of liquid.

Sometimes attacks of intermittent hydronephrosis can be terminated as well as induced by changes in posture. Occasionally a patient discovers that the attack can be relieved by lying with the head below the level of the hips. Rolling from one side to the other releases the obstruction in some cases.

Hydronephrosis of sudden onset and causing acute pain is ordinarily easily recognized and pyelograms are usually diagnostic. In a considerable number of cases, however, attacks occur only occasionally and, when the patient is free from pain, no ureteral obstruction exists and hydronephrosis cannot be demonstrated on pyelograms.

Such attacks may be accompanied by nausea and vomiting. When the episode subsides, residual soreness persists in the flank.

The pain is so severe sometimes that pyelograms are not made during the attack, yet only pyelograms

Problems relating to the recognition of hydronephrosis in everyday medical practice. Nebraska M. J. 38:17-20, 1953.

made at the time can establish the diagnosis with certainty. If no changes are seen on a pyelogram made during the episode, the kidney can be excluded as the source of pain.

Ureteral stricture and ureteral spasm are often considered the cause of sudden abdominal and flank pain. The fallacy of the diagnosis is evident if no dilatation occurs above the area in question. When the ureter is actually stenosed, the excretory urograms always reveal unmistakable dilatation above the narrowing.

Patients with this type of pain, and without pyelographic evidence of obstruction, are usually found to have spinal cord tumor, major hysteria, diverticulosis of the colon, coronary disease, cholelithiasis, protrusion of an intervertebral disk, or some other common lesion.

An insidious form of hydronephrosis occurs with partial ureteral obstruction and may be massive without causing pain or discomfort in the region of the kidney. The symptoms with this type of massive hydronephrosis are not severe and often are referred to the gastrointestinal tract.

Hydronephrosis is sometimes misdiagnosed as duodenal ulcer. A pyelogram is indicated for any young person who has dyspepsia but does not have an ulcer demonstrated on gastrointestinal roentgenograms.

Kidney Injuries in Children

H. O. MERTZ, M.D.

EXCRETORY urography is a valuable aid in the diagnosis of kidney injuries in children. When results are equivocal, injury and the degree of damage may be visualized on retrograde pyelograms. Transvesical instrumentation or surgical exploration is seldom necessary.

History of trauma, presistent loin pain, symptoms of intraperitoneal bleeding, hematuria, and discovery of an abdominal mass suggest kidney injury. Immediate prognosis is good, asserts H. O. Mertz, M.D., Indiana University, Indianapolis.

Most patients with a palpable mass are operated on. Otherwise injury to the kidney, even complete fracture, does not require immediate surgery. However, associated injury of an intraabdominal viscus demands exploration as soon as diagnosed.

Many children may be treated conservatively with satisfactory immediate results. Symptoms may subsequently develop associated with pelvic dilatation or atrophy of the kidney. Recovery may be expected after nephrectomy.

Injury of the kidney in children. J. Urol. 69:39-45, 1953.

The problem of persistent coughing in children is primarily one of diagnosis.

Chronic Cough in Childhood

A. DOYNE BELL, D.M.
Charing Cross Hospital, London

PERSISTENT coughing is probably the most common symptom in the school child. Because the cough may indicate serious and progressive disease, diagnosis is important. A careful history is essential to establish that the cough is really chronic, not the result of repeated acute respiratory infections.

Chronic upper respiratory infection—Cough from chronic upper respiratory infection may be suspected if [1] the tonsils are obviously septic, [2] the nasal airway is blocked, [3] the middle ear is repeatedly infected, [4] the paranasal sinuses are chronically infected, or [5] a mucopurulent postnasal discharge is seen. With a blocked nasal airway, the sense of smell is impaired and anorexia is common.

Early adequate treatment of acute respiratory infections prevents chronicity. A. Doyne Bell, D.M., believes that chronic tonsillar infection is the one indication for tonsillectomy. Tonsils should be examined at least four weeks after the acute infection. Tonsillectomy is advisable if pus is found in the crypts, if glands in the anterior triangle of the neck are tender, or if other evidence of continuing infection exists.

Surgical excision of tonsils and adenoids removes the site of chronic infection and establishes free drainage of the middle ear and paranasal sinuses. If the child is a mouth breather as a result of nasal obstruction, nose-breathing exercises after operation should be instituted and carried out regularly to break this habit.

Chronic paranasal sinusitis is difficult to treat. Antrum washouts, with or without antibiotic instillations, and attention to general health offer better results than radical surgery.

Bronchial infection—Bronchitis is diagnosed by hearing rhonchi and coarse or medium râles in the chest. Chronic bronchitis is almost always secondary, usually to chronic upper respiratory infection. A focus in the tonsils, sinuses, or adenoids should therefore be sought.

Collapse of lung—Obstruction of a bronchus or bronchiole by a plug of infected mucus may cause a portion of lung to collapse. In acute bronchitis, the peribronchial lymph glands are frequently enlarged and may press on the bronchi, thus contributing to the occlusion. The collapsed tissues distal to the obstruction become infected and a localized patch of pneumonitis re-

The problem of the child with a chronic cough. Practitioner 169:620-627, 1952.

sults. Segmental collapse is seen on roentgenograms. When obstruction is caused by enlarged hilar glands, tuberculosis must be considered.

When a plug of mucopus causes obstruction, postural drainage and firm thumping massage to the chest wall is usually effective. The head-down position is at first tolerated only for five or ten minutes; soon the child will retain the position for hours if allowed to play or read.

Expectorants are of doubtful help. A prophylactic antibiotic should be given to prevent pneumonitis in the collapsed tissue. If blockage continues after two or three weeks, the plug should be removed by suction through a bronchoscope.

Bronchiectasis—When the child has had one or repeated episodes of acute respiratory infection associated with physical signs of collapse or consolidation and the subsequent appearance of purulent sputum, bronchiectasis should be considered. Early diagnosis is important because, if active bronchial infection can be controlled, the natural processes of growth may considerably improve the bronchial deformity.

Full radiologic examination is warranted; the extent of damage can be assessed accurately only by bronchograms using Lipiodol.

Once the diagnosis of bronchiectasis is made, postural drainage should be instituted, varied according to the lobe or lobes affected. The output of sputum should be measured daily for a rough estimate of the effectiveness of treatment.

When extensive damage is spread through many lobes, surgery is impossible. However, if the disease is limited to 1 or 2 lobes, radical removal of the affected lobes is often advisable in established bronchiectasis. The remaining lung tissue hypertrophies in childhood and, even after resection of 2 lobes, general respiratory efficiency returns in time to almost normal.

Intrathoracic tuberculosis—With childhood tuberculosis, chronic cough is not a common symptom. When present, cough with tuberculosis is seldom productive and is probably caused by enlargement of the parabronchial or paratracheal glands.

Treatment for childhood tuberculosis is essentially the same as for the adult disease. Antibiotics should be used when ordinary measures do not bring obvious benefit.

Bronchial spasm—By interfering with flow of bronchial secretions, spasm can cause chronic cough and also predispose to bronchial obstruction and sequelae. Constant high-pitched rhonchi are heard by auscultation.

In many cases, spasm is the result of infection. Treatment of the focus, usually in the upper respiratory tract, is effective. When the child has an allergic background, the diagnosis of true allergic asthma is probably justified.

Habit—A chronic, nonproductive cough is a common habit in childhood. The child who has such a tic is often described as high strung. Intelligent handling of the basic problem by doctor, parent, and schoolteacher is necessary.

The most common hernia in infancy is inguinal which is surgically repaired if child otherwise is healthy.

Treatment of Hernias in Childhood

SAMUEL L. CRESSON, M.D.
Temple University, Philadelphia

NEARLY all hernias of infants and children are the result of preexisting congenital defects and are usually amenable to surgical therapy.

Inguinal hernias are the most common form and are ordinarily noted in the early weeks of life. The hernia may be unilateral or bilateral, being most frequent on the right side and in male infants, states Samuel L. Cresson, M.D.

The groin swelling, frequently first noticed when the child strains or cries, regresses on resting or reclining. The herniation may descend into the scrotum and gradually enlarge.

Gaining the child's confidence and cooperation aids greatly in examination. Light palpation is done over the inguinal structures with one finger. By rolling the finger from side to side, thickening of the cord on the involved side can often be elicited. A "silk glove" sensation will be felt when the sides of the hernial sac are rubbed together.

Surgical repair is advised when the diagnosis is made for an otherwise healthy child. The infant's age is of no consequence.

Adequate ligation and removal of the hernial sac are sufficient to prevent recurrence. The child is admitted on one day, operated upon the next day, and discharged the following day.

No postoperative restrictions are necessary for children under 5 years of age, except that tub baths are not permitted for a week. Progressive increase of activity is advisable for older patients.

Incarceration of an inguinal hernia is relatively common before 6 months of age. A tense, irreducible swelling is found in the inguinal region, with increasing pain. Surgical repair is done if reduction is impossible by gentle pressure or after five hours of conservative treatment utilizing sedation, elevation of the foot of the bed, and application of an icebag to the groin. When the incarceration is reduced without operation, two or three days should elapse to allow the edema to subside before herniorrhaphy.

Femoral hernias are rare in infants and children. Surgical ligation of the sac is curative.

Omphaloceles are uncommon, consisting of a herniation into the umbilical cord, and should be treated promptly. Protective moist sterile dressings are applied to the thin amniotic membrane covering to prevent drying and protect the con-

Management of hernias in infants and children. M. Clin. North America 36:1767-1777, 1952.

tents from contamination if rupture occurs. Distention of the intestines should be forestalled by Wangensteen suction and oxygen therapy.

If the defect is small, the sac may be removed immediately and the abdominal wall repaired. A large omphalocele is left intact and covered with a skin flap. Secondary repair is performed six to twelve months later.

Incarceration is rare with *umbilical hernias.* Adhesive dressings are used to pull together the muscles and fascia, since the hernia will often subside spontaneously. If the defect is over 1 cm. in diameter at 6 months of age, repair is done through a crescent-shaped incision in the inferior folds of the umbilicus, to preserve the normal appearance. After removal of the sac, the peritoneum is sutured and the fascia is closed in 2 layers. *Epigastric hernias* are treated in a similar fashion.

Congenital diaphragmatic hernias are not uncommon in the newborn and are usually seen at birth. Without surgical treatment, the mortality is extremely high.

Transitory or constant cyanosis, dyspnea, and vomiting may occur and, after a few months, the infant may fail to gain weight normally. Expansion on the affected side is decreased, and percussion reveals dullness or tympany, depending upon the type of viscera in the chest. Intestinal sounds are audible.

Roentgenograms in the flat and upright position show a mediastinal and cardiac shift, and the affected hemithorax contains a gastrointestinal pattern.

Early operation is recommended. Wangensteen suction and high concentrations of oxygen in a tent are administered both pre- and postoperatively. The diaphragm is repaired, but if the viscera have "lost the right of domicile," only the subcutaneous tissues and skin of the abdomen are closed to prevent excessive intraabdominal tension and cardiorespiratory embarrassment.

Secondary closure can be done when the infant is a week or more old.

Antibiotics and vitamin K are given until the seventh day after surgery. The child is discharged when the lung has completely expanded.

¶ CHRONIC INFANTILE ECZEMA in patients allergic to fish and unable to tolerate fish liver oils may be treated with synthetic vitamin A palmitate. A. V. Stoesser, M.D., and Lloyd S. Nelson, M.D., of the University of Minnesota, Minneapolis, observed tolerance to the drug and improvement in the skin dryness and ichthyosis for 9 patients aged 6 months to 10 years given 25,000 to 200,000 units of an aqueous dispersion of the synthetic vitamin daily for periods of three to twenty-one months; a tenth child refused to take the material, probably because of the flavoring agent added to the vehicle.
Ann. Allergy 10:703-704, 1952.

A program is presented for the application of vasodilation treatment in multiple sclerosis.

Vasodilation for Multiple Sclerosis

RICHARD M. BRICKNER, M.D.
Columbia University, New York City

SOME acute symptoms of multiple sclerosis are apparently reduced or abolished by vasodilating drugs employed before the changes have become irreversible.

Although not effective against the fundamental causes of the disease, the medications may eliminate the vasospasm and moderate the effects of the local thrombosis which produce the specific lesions, in the opinion of Richard M. Brickner, M.D., who suggests a program as a therapeutic approach requiring careful application and evaluation of symptomatic effects. Therapeutic results with multiple sclerosis are notoriously difficult to assess.

The tissue damage responsible for the acute symptoms arises from local hypoxia caused by vasospasm or thrombosis. If the blood supply can be effectively restored before irreparable damage has been done, and maintained until the unknown forces which produce the spasm or thrombosis have ceased to operate, the patient may derive remission without sequelae.

Once tissue death has occurred, no benefit can be expected from this method. Therefore, old symptoms cannot be treated successfully by vasodilating drugs.

The vasodilator employed can be one of a considerable variety, but must be a fast-acting preparation such as histamine, amyl nitrite, papaverine hydrochloride, nicotinic acid, benzazoline, or tetraethylammonium chloride.

The following treatment plan for acute episodes is suggested:

1] The response of the new symptoms to vasodilation should be tested as soon after onset as possible.

2] If the symptom is altered, the length of the effect should be learned, regardless of the duration of the flush.

3] The administration of each dose should be so scheduled as to be just before the disappearance of the previous drug's effect.

4] This schedule should be altered if necessary.

5] When acute danger is past, patients should be trained in self-administration in case a new symptom should make an appearance. Patients should always have the drug available and ready for immediate use.

6] Anticoagulation procedures must be instituted as soon as disease activity appears. These measures are to be maintained as long

Management of acute episodes in multiple sclerosis. Arch. Neurol. & Psychiat. 68:180-198, 1952.

as vasodilation treatment is continued.

7] The course of each symptom should be observed frequently and in detail. Routinization of therapy is to be avoided.

8] An ophthalmologist's services are indispensable. Frequent observation of retinal blood vessels is important to study the course of the disease and note the state of the dilation.

9] Concomitant blood pressure evaluations are necessary, and appropriate drugs should be used to offset the effects of the dilators in faintness or sudden regression.

Symptoms may not respond for the following reasons:

- New patients may be treated for symptoms which are old and no longer reversible.
- Patients may procrastinate in seeking treatment when new symptoms occur.
- The drug may have paradoxic effects and produce constriction instead of dilation. This has been noted in the retinal vessels.
- Tissue death is sometimes so rapid that treatment is precluded.
- Rapid lowering of the peripheral blood pressure may increase the hypoxia in the nervous system.

Duration of Pulmonary Carcinoma

LEO G. RIGLER, M.D., BERNARD J. O'LOUGHLIN, M.D.,
AND RICHARD C. TUCKER, M.D.

CONTRARY to the usual belief, the patient with cancer of the lung may live two or three years after inception of the disease.

Serial radiograms made in 50 cases at the University of Minnesota and Veterans Administration Hospital, Minneapolis, revealed that in operable cases the average time from start of the first symptoms or roentgen evidence to surgery was more than three years. With inoperable neoplasm the average period of survival was twenty-two and a half months.

In many cases, slow development offers a further chance of cure. Abnormality may be visible roentgenographically as long as four and a half years before onset of tumor symptoms or up to nine years before death.

Leo G. Rigler, M.D., Bernard J. O'Loughlin, M.D., and Richard C. Tucker, M.D., list 6 early radiographic changes. The most frequent and important is an enlarged and irregular hilum shadow on one side. Others are a nodular density in the lung periphery; a solitary cavity or abscess in the lung parenchyma; an area of infiltration along vascular trunks; emphysema involving a segment, lobe, or entire lung; and small areas of atelectasis, usually linear in type.

The duration of carcinoma of the lung. Dis. of Chest 23:50-71, 1953.

Angina pectoris may become the focus and point of discharge for a patient's earlier significant anxieties.

Anxiety in Angina Pectoris

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THE patient with angina pectoris is confronted with a serious danger and reacts as in other threatening situations. The resultant apprehension depends upon the effectiveness with which the customary defenses against anxiety can be utilized. Psychotherapy may produce a satisfactory adjustment both to the disease and to the anxiety.

The emotions accompanying the pain of angina pectoris are often termed angor animi, variously defined as a sense of imminent disaster, an overwhelming fear of impending death, or an actual feeling of dying. Angor animi is a misleading term, believes Jacob A. Arlow, M.D., because the anxiety associated with angina pectoris is not specific or organically distinctive.

A study of 12 angina pectoris patients who were given psychotherapy at least twice a week for not less than six months shows that dreams shed much light on the emotional reaction of the patient to the attack of angina which occurs during sleep. The dreams accompanying the angina reflect the unconscious meaning to the patient of an attack, regardless of the precipitating mechanism.

The intensity and the content of the emotional reactions to angina pectoris are determined by the previous experience of the individual and the current emotional state, varying from overwhelming panic to complete repression or denial of anxiety.

Fear of death is not always the emotion causing anxiety with angina. Abandonment and loss of love are also dreaded and may be interpreted as forms of punishment for conscious or unconscious aggressive wishes. Anxiety over the real danger of death from angina may be woven into preexisting neurotic patterns, particularly feelings of guilt.

Any awareness of a threat to the heart readily precipitates anxiety which may be combined with and enhanced by apprehensions arising from conflicts other than those connected with the immediate danger of heart failure and death. The presence or absence of anxiety during an attack of angina depends on the adequacy of the patient's characteristic psychologic defenses.

The dreams of these patients reveal that when these defenses fail, the patient experiences anxiety when waking from an attack; if defenses are adequate, the patient awakens without feeling anxious.

Anxiety patterns in angina pectoris. Psychosom. Med. 14:461-468, 1952.

Inherited tendencies seem to be the determining factors in manic-depressive psychoses among children.

Manic-Depressive Psychosis in Children

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CYCLOTHYMIC personalities and manic-depressive psychosis occur among children but are seldom described. Such cases are usually diagnosed as psychoneurosis or schizophrenia or the patients are classified as problem children. However, once having established criteria for this entity, John D. Campbell, M.D., observed 18 manic-depressive children within a four-year period.

One became psychotic at 6 years of age, and 3 others before the age of 13. Instances of manic-depressive psychoses were known in the families of 14 of the 18 cases. Often a parent was found to have had an initial attack at the same age.

The predominating symptom usually is change in mood. Ideas of reference are common, but hallucinations do not occur; such delusions as appear are not bizarre.

Youthful patients are usually taken directly to a psychiatrist, for the symptoms are predominantly emotional and psychic, though, in less severe cases, the child may be treated for anemia, parasites, run-down condition, premenstrual tension, or "adolescence."

Although suicidal ruminations are comparatively infrequent, manic-depressive disease is probably an important cause of suicide in young persons.

The patients are rarely delinquent. Such asocial behavior as is shown can be traced to depressed spirits, hypersensitiveness, the ideas of reference, or psychomotor retardation. Results of neurologic and physical examinations are essentially normal when the disease exists alone.

The pre-illness personality is important in diagnosis. Liking people, wishing to mix socially, and anxious for group approval, these children are neither schizoid, introverted, nor eccentric. Parents and teachers say that, before becoming ill, the patients often were fearful, nervous, sensitive, and insecure and had serious attitudes toward life with strong drives to succeed. Mood swings are prominent. Symptoms are not used as a means of evading responsibility.

Intelligence is somewhat above average. Literary work, organizational and social activities are usually preferred to sports. Many of the children are successful in extracurricular school activities. Too much strain and responsibility are often considered the most important precipitating factors.

Manic depressive psychosis in children. J. Nerv. & Ment. Dis. 116:424-439, 1952.

In most instances no dynamic or environmental factors account for the development of the illness. No traumatic experiences can be shown to have caused the breakdown. Home life and relationships are usually good.

Patients fail to improve with psychotherapeutic procedures or the removal of alleged environmental factors, revealing the endogenous nature of the condition. Incapable of self-analysis, the children are cooperative, but not introspective, and are bored by attempts to arouse psychiatric insight.

If the condition is not severe, rest, relaxation, slight sedation, and vitamins are usually sufficient therapy.

Electroshock is specific in severe episodes.

Prognosis depends more upon the cyclothymic disposition of the individual than upon the age at the first manifestation. Some patients never become completely normal. Depression may recur later or alternated with hypomania. The intervals between episodes and the severity of the attacks are definitely related to inherited tendencies.

New Theory of Ménière's Disease

JULIUS LEMPERT, M.D., AND ASSOCIATES

CHRONIC progressive herpetic neuritis of the vestibular labyrinth may be responsible for Ménière's syndrome. Julius Lempert, M.D., Dorothy Wolff, Ph.D., and J. H. T. Rambo, M.D., of the Lempert Research Foundation, New York City, and Ernest Glen Wever, Ph.D., and Merle Lawrence, Ph.D., of Princeton, N. J., derive this explanation from histologic changes observed in specimens obtained during operation and autopsy.

An attack of Ménière's disease is caused by rupture of one or more vesicles, with release of toxic fluid into the lumen of the endolymphatic labyrinth. Vesicles form and break periodically, the size and number determining the intensity of paroxysms.

All symptoms may be the result of contamination of the endolymph. Violent vertigo is due to irritation of the crista by discharged liquid and not to increased pressure.

However, pressure is raised, so that the chochlear duct is distended and the delicate membrane of Reissner bulges or ruptures.

Tinnitus and cumulative loss of hearing in the course of the disease result from overstimulation and injury of Corti's organ by repeated contamination of the endolymph. Deafness represents toxic loss of function in the hair cells; symptoms gradually subside as harmful fluid is resorbed.

New theory for the correlation of the pathology and the symptomatology of Ménière's disease. Ann. Otol., Rhin. & Laryng. 61:717-746, 1952.

Symposium

Autonomic Drugs: An Introduction

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Prepared for Modern Medicine

IT has been established that epinephrine and norepinephrine jointly constitute the neurohormone of the sympathetic division of the autonomic nervous system. Acetylcholine plays a similar role in the parasympathetic division of the autonomic nervous system. The phytion, acetylcholine is responsible for the transmission of the nerve impulse across the synapse from the pre- to the postganglionic fibers in each division of the autonomic nervous system.

Based upon these physiologic facts, many new drugs have been developed in the last two decades which have played an important role in clinical medicine. These drugs have been designed to emulate the activity of one of the neurohormones, such as the sympathomimetic amines. Among these are the important drugs neosynephrine and ephedrine. Others have been designed to emulate the hormonal influence of acetylcholine. Such are Mecholyl and Urecholine.

In addition, drugs have been designed to antagonize or block the activity of the neurohormones in the sympathetic division of the autonomic nervous system. In addisician has available such adrenergic blocking agents as Priscoline and Regitine.

In the parasympathetic division of the autonomic nervous system the old reliable atropine remains as one of the most useful drugs in the blocking of the action of acetylcholine. Added to it, however, is a formidable list of synthetic anticholinergic drugs that are proving useful in many conditions where spasmolytics are required.

Other important additions to the armamentarium of the physician, based upon activity on the autonomic nervous system, are those agents which block specifically autonomic ganglia. Recently the introduction of hexamethonium bromide in the treatment of hypertension represents an application of this principle.

The interesting papers by Drs. Yonkman, Grollman, and Ahlquist in this volume demonstrate that the physician's armamentarium in the treatment of many diseases has been augmented by the addition of drugs which affect the autonomic nervous system.

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First of a Series

The Autonomic Nervous System and Hypertension

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Prepared for Modern Medicine

THE voluminous literature which has accumulated in recent years on the use of various autonomic drugs in the treatment of hypertension is evidence of the avidity with which useful medicaments for this common disease are sought. Practically every drug that has the capacity to paralyze either the sympathetic ganglia or the autonomic nervous system has been advocated for this purpose.

Among the earlier ones utilized were the veratrum preparations. These were followed by ergotoxine derivatives and by tetraethylammonium derivatives. Recently interest has centered on hexamethonium and hydrazinophthalazine derivatives. Almost without exception unwarranted claims have been made for each of these products, suggesting that here at last was a solution to the medical management of hypertension.

With more critical evaluation, these extravagant claims have been found unwarranted. A more rational approach has indicated the limitations, if not the entire uselessness, of the compounds in the practical management of hypertension. It is probable that their side effects exceed their potential value in the treatment of slight or moderate hypertension. However, they may have a definite indication when properly used in hypertensive crises and malignant hypertension. Meanwhile, careful work by critical and objective observers must be awaited before drawing any final conclusions.

Blood Pressure Mechanism

The mean arterial blood pressure is determined by the cardiac output and the arteriolar resistance. The latter, in turn, is regulated by a variety of local and reflex hormonal and nervous mechanisms.

These nervous influences operate through the autonomic nervous system. The activity of the sympathetic division of the autonomic nervous system tends to increase the resistance, while activity of the parasympathetic system, with its

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outflow through the dorsal roots, tends to decrease the resistance. These nervous influences affect the peripheral resistance in response to stimuli originating in local areas or through central regulating mechanisms, such as the buffer—carotid sinus and aortic arch—nerves and vasomotor center.

Neurogenic Hypertension

Denervation of the carotid sinus and aortic arch in dogs has been shown repeatedly to result in an elevation in blood pressure. This has been designated neurogenic hypertension in contrast to the renal hypertension induced by manipulation or removal of the kidney or its blood supply. However, it must be emphasized that this so-called "neurogenic" hypertension differs fundamentally from renal hypertension and from the hypertensive cardiovascular disease occurring in human beings.

In renal experimental hypertension, as well as in hypertension in human beings, the peripheral resistance is increased generally throughout the body while the cardiac output remains normal. In neurogenic hypertension, as observed experimentally, both the heart rate and blood pressure are labile, tending to return to normal with exercise and basal conditions. The blood flow is shunted away from areas with active vasoconstrictor mechanisms.

To what extent neurogenic hypertension of this type actually occurs as a clinical entity in man is not well established, although lability of blood pressure under nervous influences is, of course, commonly encountered. That sympathetic nervous pathways mediating neurogenic vasoconstriction are not the only mechanism whereby an elevation in blood pressure may be maintained is evident from the fact that total sympathectomy usually fails to reduce blood pressure to normal.

Autonomic Drugs

Demonstration of the important role played by the autonomic nervous system in the maintenance of blood pressure led early to the belief that abnormalities in autonomic control were responsible for the elevations in blood pressure observed in hypertension and that interference with the sympathetic nervous system would in turn affect the blood pressure. Despite the obvious simplicity of this theory, there is little to support the concept that abnormalities in sympathetic activity are in any way responsible for the development of hypertension.

It is true that lesions in the central nervous system may cause an elevation in blood pressure and that, as stated, removal of the buffer nerves in animals will produce a rise in blood pressure, but such elevations are not true hypertensive cardiovascular disease. This erroneous assumption probably accounts for the lack of success in the treatment of hypertension by removal of the autonomic innervation of the blood vessels either surgically, as by sympathectomy, or by the use of drugs with a sympatholytic or autonomic blockading action.

With the emphasis on the autonomic nervous system as affecting the blood pressure, a variety of drugs that affect the autonomic nervous system has been utilized in the treatment of hypertension. In view of a demonstrated capacity to lower normal as well as elevated blood pressure, it was assumed that these compounds would be effective in the treatment of hypertension.

Unfortunately, this simple hypothesis has not proved correct and, although the drugs have actually reduced the blood pressure, the undesirable side effects accompanying such reductions have in most cases rendered their use of questionable value in therapeutics. Hypertensive cardiovascular disease is not synonymous with an elevation in blood pressure but is a specific disorder in which a rise in diastolic pressure from increased peripheral resistance is only one manifestation. Under certains conditions, accordingly, reduction in the blood pressure in hypertension may actually be harmful to the patient.

Veratrum Preparations

Preparations of veratrum viride have been recommended and used widely in therapy of hypertension but have recently fallen into disrepute. Their hypotensive response is a result primarily of a vasodilator reflex, the afferent pathway of which arises in the vessels of the heart and lungs and runs in the vagus nerves with the efferent vasodilator fibers distributed through the sympathetic.

The activity of extracts of veratrum results from a number of alkaloidal principles which are closely related chemically and pharmacodynamically. Several purified fractions have been marketed with the hope that these might retain the desired hypotensive activity with fewer side effects.

Except for the greater exactitude in dosage possible by using pure principles, little advantage has been demonstrated over the cruder preparations that were employed earlier.

Nausea, vomiting, and other serious side reactions, inconstant effects on the blood pressure level, and the development of tolerance to the hypotensive action of the drugs have militated against acceptance of veratrum preparations in the therapy of hypertension.

The various preparations have been administered orally or parenterally with gradually increasing dosage to mitigate the side effects. The parenteral solutions are given intravenously for short periods only in hypertensive crises.

Ergotoxine Derivatives

Stoll's discovery that partial reduction by hydrogenation of the alkaloids of the ergotamine and ergotoxine groups of ergot derivatives decreases the capacity of these drugs to stimulate smooth muscle, and increases their adrenergic blocking activity, suggested use of these alkaloids in treatment of hypertension.

Hydergine, a mixture of equal parts of the 3 hydrogenated alkaloids of the ergotoxine group—dihydroergocornine, dihydroergocristine, and dihydroergokryptine—

has been shown to lower vascular tone by central action, by direct peripheral adrenergic blockade, and by capacity to dampen pressoreceptor reflexes. A number of observers have reported slight decreases in the blood pressure, an average of about 30 mm. systolic and 15 mm. diastolic, in half the patients in whom the drug was tried.

As with other agents of this group, side effects—nausea, vomiting, and a feeling of tiredness, with aching and flushing of the head—are often noted. Because of these side effects, as well as relative ineffectiveness as hypotensive agents, the ergotoxine derivatives have not received wide acceptance and have been largely superseded.

Ganglionic Blocking Agents

Autonomic blockade may be accomplished by drugs acting peripherally or on the ganglia in which the nerve fibers synapse. Ganglionic blocking agents and sympatholytic and adrenolytic agents have been proposed and used in treatment of hypertension.

Among the first ganglionic blocking agents to be tried were tetraethylammonium compounds which, as Burn and Dale in 1915 showed, had the capacity to blockade autonomic ganglia. Although these compounds were capable of lowering the blood pressure acutely, their use in hypertension was soon found to be severely limited by the transitory nature of the depressor effect and the undesirable side reactions. Employment in this disorder was soon abandoned.

Hexamethonium Compounds

The most recently introduced ganglionic blocking agents are the hexamethonium compounds which Paton and Zaimis in 1948 showed had blocking effects similar to those of tetraethylammonium salts but 10 to 20 times as potent and much longer lasting. Both the penta- and hexamethonium derivatives have been tried in essential hypertension.

The reports are rather contradictory and final conclusions regarding the value of these compounds must await more critical studies. Several observers have noted remissions of malignant hypertension but in many cases progress of the disease has not been altered.

In addition to the postural hypotension and the other side effects induced by all members of this group of drugs, azotemia, secondary to the reduction in the glomerular filtration rate and decreased blood flow through the kidney, is a serious side reaction and may render use of the hexamethonium derivatives dangerous.

The hexamethonium compounds are available for parenteral as well as oral administration. For intramuscular injection the bromide is marketed in a solution containing 20 mg. per cubic centimeter. Therapy is best initiated with very small doses, not exceeding 5 mg., because rather alarming symptoms may follow the use of larger doses in some individuals.

For oral administration, the chloride rather than the bromide is used in order to avoid bromide intoxication, since much larger doses are

necessary with this route of administration. The absorption of hexamethonium compounds from the gastrointestinal tract is apparently erratic since the ratio of effective doses by oral and parenteral routes is enormous.

Experience with the methonium compounds is still too inadequate for final evaluation, despite the fact that the agents are generally available and widely utilized. Many studies are unconvincing because of the difficulty of determining the efficacy of compounds for a chronic disorder in which the blood pressure is labile and subject to variation through many influences.

For example, Lockett, Swan, and Greive found the methonium compounds hardly more effective than bed rest for lowering blood pressure. When administered orally the drugs failed completely to lower the blood pressure of ambulatory patients. The sedative effect of the bromide salts of the drugs used in the earlier studies undoubtedly contributed to the subjective improvement noted.

Several investigators have found oral hexamethonium entirely without effect and have therefore limited the use of the drug to parenteral administration in the management of hypertensive crisis. The careful study of Werkö indicated that, although hexamethonium compounds exerted a definite depressor effect far superior to the insignificant action induced by tetraethylammonium bromide or the barbiturates, a tolerance was produced so rapidly that the material was of little value for routine therapy of hypertension.

Werkö concluded that the drug induces effects by producing a pooling of blood in the systemic circuit with a decreased cardiac output and renal blood flow and an increased pulse rate. In general, the systolic pressure is affected considerably more than the diastolic. An inconsistency was also found between the size of the dose and the depressor response. These conclusions have been confirmed by other workers.

Hydrazinophthalazine

The hypotensive action of a number of derivatives of hydrazinophthalazine was noted by a group of Swiss investigators. Of these compounds, 1-hydrazinophthalazine has been most widely used. Rather enthusiastic reports of the effectiveness of this compound in lowering the blood pressure of hypertensive patients have appeared and the drug is now marketed as Apresoline.

Apresoline, unlike hexamethonium, is absorbed efficiently from the gastrointestinal tract. The agent is usually administered in enteric-coated tablets in doses of 25 and 50 mg. one to four times daily. In hypertensive crisis, the compound may be given parenterally in doses of 5 to 20 mg.

It is still undecided whether Apresoline exerts a central action, but many of the side effects elicited by the drug, as well as some experimental studies, suggest this possibility.

The principal mechanism is a peripheral sympatholytic action. Severe headache, nausea, and vom-

iting are not infrequently noted after use of the drug, so that therapy should be initiated cautiously.

Some have recommended the use of Apresoline in conjunction with hexamethonium salts—the latter compound being given parenterally, the former orally. There is no good evidence to show any synergy of the two drugs or advantages of the combination. The early extravagant claims of the possibility of maintaining the blood pressure at normal levels by the combined use of the drugs have not been confirmed by more carefully controlled studies.

Therapeutic Use

In view of the remarks at the beginning of this paper regarding the role of the autonomic nervous system in the pathogenesis of hypertension, the question arises as to the advisability, indications, and value of the drugs under discussion. Although the use of depressor agents does not affect the basic disorder in hypertension, nevertheless there is believed to be some advantage in lowering the blood pressure which, if not responsible, at least contributes to the sequelae of the disease, such as the cardiac failure, cerebral vascular accidents, and arteriolar sclerosis.

The basic problem has been to obtain drugs which lower the blood pressure without causing undue side reactions. Unfortunately, this goal has not yet been attained. At best, the drugs may be of value in reducing the excessive elevations noted during attacks of the so-called hypertensive crisis and in hypertensive encephalopathy which characterizes the malignant phase of hypertension. Value of the drugs in these conditions, however, must still be considered to be in an experimental stage.

Both Apresoline and hexamethonium as well as the other drugs of this series must be used with caution. Several deaths have followed the use of these drugs. It is obvious that any drug which tends to lower the blood pressure may induce cerebral and myocardial ischemia and thus cause fatal consequences.

A rising concentration of the blood urea nitrogen is often noted during medication with hexamethonium and certain other hypotensive agents because of the decreased renal plasma flow and glomerular filtration rate induced. This effect on the renal plasma flow does not occur with hydrazinophthalazine.

Any of these drugs should be used with extreme caution for patients with coronary artery disease, renal insufficiency, or an existent or incipient cerebral vascular accident.

Second of a Series

The Sympathomimetic Agents

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Prepared for Modern Medicine

THE sympathomimetic agents are drugs which induce physiologic responses similar to those produced by the postganglionic adrenergic nerves. Impulses transmitted over these nerves release a chemical mediator, sympathin, at the neuroeffector junctions.

Sympathin, acting through a specialized receptive mechanism of the effector cells, evokes the characteristic effector response. This receptive mechanism, termed the adrenotropic or adrenergic receptor, is presumed to be the site of action of the sympathomimetic agents. The hormone of the adrenal medulla may be considered to be an endogenous sympathomimetic agent.

Chemically, most of the sympathomimetic drugs are derivatives of phenylethylamine. In the table appended to this article are listed generic, trade-marked, and chemical names of 24 of the most commonly used substances.

Epinephrine, arterenol, isopropylarterenol, and ephedrine will be considered in some detail since all the others are similar in action, and so in use, to one of these.

EPINEPHRINE

The responses evoked by epinephrine, the prototype sympathomimetic agent, are complex, depending on species, dose, and route of administration.

Smooth muscle—Some smooth muscle responds by contraction and other by relaxation and some has no significant response to epinephrine.

The muscle of the dilator portion of the iris, the orbit, the gastrointestinal sphincters, the biliary ducts, the splenic capsule, the pilo-erectors, the myometrium of many species, and the blood vessels of the skin, mucous membranes, and viscera contract in response to epinephrine.

The bronchial smooth muscle, that of the gastrointestinal tract generally, the myometrium of a few species, and some blood vessels—those in skeletal muscle and perhaps the coronaries—relax in the presence of epinephrine.

The sphincter of the iris and the ciliary muscle are not significantly affected by epinephrine.

Heart—Epinephrine has three distinct effects on the heart. The

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rate is increased, the myocardium contracts more vigorously, and the rhythm is disturbed by ventricular extrasystoles and potential ventricular fibrillation. The latter effects are more pronounced in the presence of cyclopropane and chloroform.

The effects of epinephrine on cardiac output, arterial pressure, and peripheral resistance in man are complex. A low concentration infused into the femoral artery produces vasodilation in the leg. A low concentration infused intravenously decreases peripheral resistance and increases heart rate and cardiac output. Because of the cardiac stimulation, the systolic and mean pressures usually rise in spite of the decreased peripheral resistance. The diastolic pressure may decrease, increase slightly, or remain unaffected.

Vasoconstriction is also present, as indicated by the blanching of the skin.

It can be demonstrated that epinephrine is a ganglionic blocking agent and that it produces a depressor response probably by some direct action in the central nervous system. The significance of these effects in man is unknown.

Glands—Not all exocrine glands respond to epinephrine. Lacrimal, nasopharyngeal, bronchial, and gastrointestinal glands are practically unaffected except indirectly through vascular changes. The salivary glands produce a sparse, thick secretion under the influence of epinephrine.

Epinephrine in the liver induces glycogenolysis and a transient hyperglycemia.

One endocrine gland responds to epinephrine. The anterior pituitary releases adrenocorticotropic hormone either as direct response to epinephrine or as a response mediated through the hypothalamus.

Metabolism—Epinephrine will increase the oxygen consumption of the whole body without affecting the respiratory quotient. The exact mechanism of this calorigenic effect is unknown; evidence that it is due to a specific metabolic action is balanced by evidence that it is due to hyperglycemia and cardiovascular changes.

Toxicity—Epinephrine produces toxic effects characterized by central nervous system and cardiovascular symptoms. Anxiety and apprehension, together with headache, cardioacceleration, palpitation, pallor, and tremor, are the most commonly observed toxic effects.

The principal contraindications to the use of epinephrine are hyperthyroidism, cardiac dilatation, and coronary disease. Caution should be used in the presence of hypertension.

Fate—Epinephrine and the other dihydroxyphenyl compounds are unstable. Solutions are preserved by the addition of reducing agents such as sodium bisulfite or ascorbic acid.

The exact fate of epinephrine in the body is not yet clearly understood. It is rapidly inactivated by a variety of enzymatic reactions; it may be conjugated with sulfuric acid or destroyed by amine oxidase. There is evidence that the liver is the primary site of inactiva-

tion; however, other tissues may also play a role.

Administration—Epinephrine can be administered topically as a 0.1% solution or injected subcutaneously or intramuscularly in the same concentration or intramuscularly as a 0.2% suspension in oil. The latter preparation is intended for prolonged action.

The bronchospasm of asthma may be relieved by inhalation of a nebulized 1% solution.

Orally, epinephrine has practically no effect because of gastrointestinal inactivation, poor absorption, or rapid destruction in the liver.

Uses—The principal therapeutic uses for epinephrine are as follows:

- To relieve bronchospasm and bronchial congestion in bronchial asthma
- To treat urticaria, angioneurotic edema, and vascular collapse in allergic and anaphylactic states
- To confine and prolong intradermal, subcutaneous, and spinal effects of local anesthetics. No other sympathomimetic agent is as potent as epinephrine in this regard.
- As a decongestant and mydriatic in the eye. These actions are potentiated by cocaine.
- By local application, to control capillary bleeding
- As a nasal decongestant. A rebound congestion often occurs because of either reactive hyperemia or residual direct vasodilation.
- To relax constriction rings of the uterus at term. Low doses administered subcutaneously are preferable, since high dosage may cause uterine contraction.
- As an emergency measure in insulin hypoglycemia. Epinephrine is not effective if the glycogen stores of the liver are insufficient.
- To stimulate the myocardium in acute cardiac arrest
- To test the anterior pituitary–adrenal cortex function.

Arterenol

The primary amine, arterenol, has been known and studied for over four decades. Recently, racemic arterenol has been resolved into the levorotatory isomer and introduced into clinical practice as Levophed. The agent is likewise known as norepinephrine or noradrenaline.

Arterenol is qualitatively similar to but quantitatively different from epinephrine. In man, epinephrine is more active in all respects than arterenol. Exceptions to this rule occur in some other species.

Arterenol is 2 to 10 times less active than epinephrine as a vasoconstrictor, mydriatic, uterine stimulant, and gastrointestinal relaxant. It is 10 to 100 times less active as a vasodilator, bronchial relaxant, uterine relaxant, or myocardial stimulant. In addition it has only very slight activity in producing glycogenolysis and the release of ACTH. Its toxicity is much less than that of epinephrine.

The effects of arterenol when administered by slow intravenous infusion illustrate the quantitative differences from epinephrine. A dose of 2 to 5 μg. per minute increases the systolic, diastolic, and mean arterial pressures. The heart is slowed by vagal inhibition and the cardiac output diminished because of the increased peripheral resistance. As stated, epinephrine in similar dosage increases the arterial pressure by cardiac stimulation and at the same time reduces the peripheral resistance. Although these results have been interpreted by some as indicating that arterenol

is a better vasoconstrictor than epinephrine, the proper interpretation is that arterenol is a less active vasodilator and myocardial stimulant.

The lack of dilator action by arterenol is also demonstrated by the fact that the adrenergic blocking agents do not cause it to produce a depressor response. The pressor action of arterenol is diminished, but not usually reversed, by this type of blocking action. Intra-arterial infusions of arterenol produce only vasoconstriction in the human leg whereas epinephrine produces vasodilation.

As compared with epinephrine or isopropylarterenol, arterenol has practically no effect on cardiac rhythmicity in human beings. It is therefore of no value in treating cardiac arrest.

The principal use for arterenol is in the maintenance of arterial pressure during hypotensive episodes. The compound is administered by continuous intravenous infusion.

Although less active than epinephrine as a vasoconstrictor, arterenol used with the local anesthetics gives satisfactory results. A higher concentration is necessary, but the toxic effects associated with epinephrine are not produced.

Sympathin is probably a mixture of arterenol and epinephrine. Arterenol has been identified as the principal adrenergic neurohormone, while epinephrine is the principal hormone of the adrenal medulla. The comparative potencies of the two amines suggest a relationship between the adrenergic nerves and the adrenal medulla.

During periods of comparative inactivity, the adrenergic nerves carry on normal regulatory functions such as maintaining pupil size, vasomotor tone, and heart rate. Arterenol is effective for these ordinary functions.

In anger, excitement, or fright a generalized discharge of the sympathoadrenal system occurs. The epinephrine released from the adrenal medulla reinforces the effects of arterenol from the adrenergic nerves.

The greater the proportion of epinephrine in any mixture of epinephrine and arterenol, the more effective the combination is in bringing about the responses associated with sympathetic discharge. For example, epinephrine by stimulating the heart and producing vasodilation in skeletal muscle gives the proper redistribution of blood during periods of emergency.

In fact it can be shown, in animals at least, that epinephrine evokes responses which cannot be reproduced by adrenergic nerve stimulation. Any mixture of epinephrine and arterenol, therefore, would be more physiologically efficient than arterenol alone.

In pheochromocytoma the extract of the excised tumor usually contains more arterenol than epinephrine. This is not strict proof that the secretion of the tumor in situ is mainly arterenol. Whether it is or not makes little difference in diagnosis of pheochromocytoma with adrenergic blocking agents since the pressor effect of arterenol is blocked by these drugs just as effectively as that of epinephrine.

Isopropylarterenol

The sympathomimetic agent, isopropylarterenol, available commercially under such names as Norisodrine, Isonorin, Isuprel, and Aludrine, is more potent than epinephrine as a vasodilator, bronchial and uterine relaxant, and myocardial stimulant. It is much less active than epinephrine in all other respects.

The arterial pressure in man is variably affected by isopropylarterenol. The diastolic and mean pressures usually fall because of the decrease in peripheral resistance. The intense myocardial stimulation may increase the systolic pressure. Tachycardia is always produced. There is symptomatic and electrocardiographic evidence of coronary insufficiency. Caution should be observed if patients have cardiac disease.

Because of its cardiac action, isopropylarterenol is not indicated as a hypotensive agent. It could, however, be used to treat acute cardiac arrest.

Bronchial asthma is the primary indication for this drug. It is inhaled as a nebulization, oxygen-aerosol, or dust. Systemic effects occur most often with the last method. Sublingual administration is often effective. Since this drug lacks the decongestive action of epinephrine, the use of a substance such as phenylephrine simultaneously, or epinephrine alternately, may be necessary in some cases.

Ephedrine

Historically, ephedrine ranks second to epinephrine. The researches which have introduced the many sympathomimetic agents into clinical practice stemmed from the discovery of the nature, structure, and uses of this alkaloid.

The nonphenolic compounds, of which ephedrine is the prime example, are less potent than epinephrine. However, they are more resistant to inactivation and so have prolonged action and are effective by oral administration.

Ephedrine has at least two mechanisms of action. It acts directly on the adrenotropic receptors in a manner similar to epinephrine, and it potentiates the actions of naturally occurring sympathin or epinephrine. Tachyphylaxis develops with repeated administration.

In many respects ephedrine is the one sympathomimetic agent which most nearly duplicates the effects of epinephrine. Although it requires much larger doses than those required of epinephrine, ephedrine is a good vasoconstrictor and mydriatic.

Ephedrine is a relatively good nasal decongestant. However, as with epinephrine, rebound congestion often occurs. Ephedrine is effective in correcting and preventing the hypotension of spinal anesthesia.

Many cases of bronchial asthma can be controlled with ephedrine. Its effectiveness is due in part to vasoconstriction producing decongestion and in part to a potentiating effect on adrenergic activity.

The isopropylamines are potent corticomedullary stimulants. When ephedrine is used as a sympathomimetic agent this is generally con-

sidered to be an undesirable side action. The simultaneous administration of a short-acting barbiturate is often indicated. Many of the newest sympathomimetic agents are selected because they do not produce this central stimulation.

Other Sympathomimetics

Ethylnorepinephrine—This dihydroxyphenyl, known also as Butanephrine, resembles isopropylarterenol in action, is an effective bronchodilator, and produces cardiac stimulation and peripheral vasodilation.

Its principal use is in the treatment of bronchial asthma. A dose about twice that of epinephrine is required.

Ethylnorepinephrine has an interesting effect in animals. The first intravenous dose produces a marked fall in arterial pressure. Subsequent doses, if administered at frequent intervals, produce increasing pressor responses. It is not known whether this reaction occurs in man.

Like isopropylarterenol, Butanephrine should be used with caution if signs of coronary insufficiency are present.

Phenylephrine and sympatol—Phenylephrine (Neosynephrine), as well as its close chemical relative sympatol, are arterenol-like amines. Their effects are comparable except that the former is more potent. Phenylephrine is more widely used.

Vasoconstriction without cardiac stimulation, and mydriasis without cycloplegia are the primary actions of clinical use.

In hypotensive states, as during spinal anesthesia, small repeated intravenous doses efficiently maintain the arterial pressure. In orthostatic hypotension and in many allergic states, phenylephrine by mouth acts as a systemic vasoconstrictor.

The reflex vagal slowing produced by the acute pressor response to intravenous phenylephrine is often effective in arresting paroxysmal supraventricular tachycardia. If the pressure does not rise, slowing does not occur.

Like arterenol, phenylephrine can be used with local anesthetics when the toxic effects of epinephrine are undesirable. A 0.5% solution in buffered saline is a good nasal decongestant. Resistance and rebound congestion do not often occur.

A variety of preparations of phenylephrine are available for use as mydriatics. The stronger solutions may cause corneal irritation, so local anesthetics, except butacaine, which is incompatible with chlorides, are often added.

The monohydroxyphenyl compounds are not as unstable as the dihydroxy analogues. An approximately equivalent response will be obtained with phenylephrine, using 0.5 mg. intravenously, 5 mg. subcutaneously, or 250 mg. orally.

These amines do not produce central stimulation. Hence, any toxic effects are cardiovascular in origin.

Hydroxyamphetamine, methoxamine, and cyclopentamine—These amines, known respectively as Paredrine, Vasoxyl, and Clopane, are classified as arterenol-like sympathomimetics. Their general actions

and uses are the same as those described for phenylephrine.

They do not produce central stimulation, are active vasoconstrictors, and are used as nasal decongestants and antihypotensive agents. Paredrine is occasionally used as a mydriatic.

Mephenteramine and Oenethyl—Although chemically dissimilar, mephenteramine (Wyamine) and Oenethyl resemble phenylephrine in action. They are used primarily as antihypotensive agents during spinal anesthesia.

Phenylpropanolamine, Amphetamine, and Methamphetamine—These are ephedrine-like sympathomimetic amines. All are active corticomedullary stimulants. Since phenylpropanolamine (Propadrine) is the least active in this respect, it is the one used primarily as a nasal decongestant, in that the anxiety complex so often associated with the others is not so likely to occur.

Amphetamine (Benzedrine) and its dextrorotatory isomer, Dexedrine, are more often used as central stimulants than as sympathomimetic agents. But amphetamine is a nasal decongestant and is used to treat orthostatic hypotension.

Methamphetamine, also known as desoxyephedrine, and available under many different trade names, differs little from amphetamine. It is used as a nasal decongestant, an antihypotensive agent, and a central stimulant.

When these amines are used as central stimulants their sympathomimetic effects are often looked upon as undesirable side actions.

N-ethyl ephedrine—Nethamine is a tertiary amine related chemically and also pharmacologically to ephedrine. Its effects on the cardiovascular and central nervous systems are minimal. It is a fairly good smooth muscle relaxant. Nethamine is used in bronchial asthma and other forms of allergy and in some types of dysmenorrhea.

Methoxyphenamine—This amine, known as Orthoxine, is another ephedrine-like compound which has minimal action on the cardiovascular and central nervous system. It is used primarily in allergic conditions in which a hypertensive agent would be undesirable.

Phenylpropylmethylamine and tuaminoheptane—Vonedrine and Tuamine are ephedrine-like compounds which lack central stimulant effects. Both are used exclusively as nasal decongestants.

Their free bases are volatile and are used in inhalers, while their water-soluble salts are used in solution for local application.

Benzedrex and methylhexaneamine—These are ephedrine-like compounds which do not produce significant central stimulation. They are volatile amines used in inhalers. Benzedrex was introduced solely to replace Benzedrine in inhalers.

Naphazoline—Privine is a potent sympathomimetic vasoconstrictor. It is an imidazole derivative related pharmacologically to ephedrine. It does not produce central stimulation.

Privine is used exclusively as a nasal decongestant in low concentrations, 0.05 to 0.1%. Rebound congestion, probably due to reac-

SYMPATHOMIMETIC AGENTS

Generic & Trademarked Names	Chemical Names
ARTERENOL, norepinephrine, noradrenaline, Levophed ®	*3,4-Dihydroxyphenyl-* -ethanolamine
EPINEPHRINE, adrenaline, Adrenalin ®, Suprarenin ®	-ethanol-methylamine
ISOPROPYLARTERENOL, Isuprel ®, Norisodrine ®, Isonorin ®, Aludrine ®	-ethanol-isopropylamine
ETHYLNOREPINEPHRINE, Butanephrine ®	-butanolamine
SYMPATOL, Synthenate ®	*4-Hydroxyphenyl-* -ethanol-methylamine
HYDROXYAMPHETAMINE, Paredrine ®	-isopropylamine
PHENYLEPHRINE, Neosynephrine ®	*3-Hydroxyphenyl-* -ethanol-methylamine
METHOXAMINE, Vasoxyl ®	*2,5-Dimethoxyphenyl-* -isopropylamine
METHOXYPHENAMINE, Orthoxine ®	*2-Methoxyphenyl-* -isopropyl-methylamine
PHENYLPROPANOLAMINE, Propadrine ®	*Phenyl-* -isopropanolamine
EPHEDRINE	-isopropanol-methylamine
N-ETHYL EPHEDRINE, Nethamine ®	-isopropanol-methylethylamine
AMPHETAMINE, Benzedrine ®	-isopropylamine
METHAMPHETAMINE, desoxyephedrine, Desoxyn ®, Norodin ®, Amphedroxyn ®, etc.	-isopropyl-methylamine
MEPHENTERAMINE, Wyamine ®	*-tertiary*-butyl-methylamine
PHENYLPROPYLMETHYLAMINE, Vonedrine ®	-propyl-methylamine
BENZEDREX ®	*Cyclohexyl-* -isopropylamine
CYCLOPENTAMINE, Clopane ®	*Cyclopentyl-* -isopropyl-methylamine
NAPHAZOLINE, Privine ®	*-imidazoline* Naphthyl-methyl-
BENZAZOLINE, Priscoline ®	Benzyl-
	Aliphatic amines
TUAMINOHEPTANE, Tuamine ®	2-Amino-heptane
METHYLHEXANEAMINE, Forthane ®	2-Amino-4-methyl-hexane
METHYLOCTYLAMINE, Octin ®	2-Methylamino-iso-octene
OENETHYL ®	2-Methylamino-heptane

The above sympathomimetic agents are generally used in the form of water-soluble salts, such as the hydrochloride, hydrobromide, sulfate, or tartrate. Arterenol, epinephrine, phenylephrine, ephedrine, and N-ethyl-ephedrine are usually used as the levorotatory isomers.

tive hyperemia, which may occur is prevented in some cases by using a more dilute solution.

Benzazoline—Another imidazole derivative, Priscoline, is included in this discussion because some of its actions resemble those of isopropyl-arterenol. In many species, including man, Priscoline is a direct myocardial stimulant. Some of its vasodilating action may also be sympathomimetic in nature.

Actually the pharmacologic actions of this drug are very complex. In addition to being an adrenergic blocking agent, it also has effects

like those of both histamine and acetylcholine.

Methyloctylamine—Octin, an unsaturated aliphatic amine, can be considered an ephedrine-like drug. In some circumstances it acts as a vasoconstrictor; however, it appears to be a direct smooth muscle relaxant. Octin is used primarily in renal colic and dysmenorrhea.

Prediction of Response

A theory regarding the nature of the interaction of the sympathomimetic agents and the adrenotropic receptor has been developed in this laboratory. According to this concept there are two kinds of receptors. One, known as the *alpha* receptor, is associated with vasoconstriction, mydriasis, splenic, myometrial, and pilomotor contraction, and intestinal inhibition. The other, the *beta* receptor, is concerned with vasodilation, bronchial and myometrial inhibition, and myocardial stimulation.

The chemical structure of the sympathomimetic agent determines which of the receptors will be activated and to what degree. The receptor determines effector response.

Arterenol acts primarily on the *alpha* receptor and brings about the responses. Isopropylarterenol acts on the *beta* receptor.

Epinephrine acts on both receptors and produces *all* of the adrenergic responses. There is probably no complete epinephrine substitute. Each of the other sympathomimetic agents will produce only some of the effects of epinephrine.

By classifying the rest of the sympathomimetic agents as to which receptor they activate predominantly, the type of response can be anticipated. Among the *alpha* activators we would name phenylephrine, hydroxyamphetamine, and methoxamine. *Beta* activators would include ethylnorepinephrine, benzazoline, and methoxyphenamine.

Although this theory is obviously not perfect, it does indicate that there is a way to predict the total effects of sympathomimetic agents.

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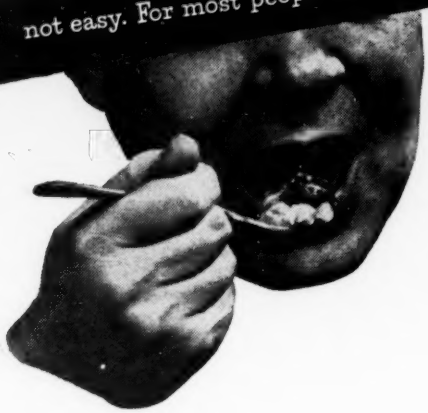

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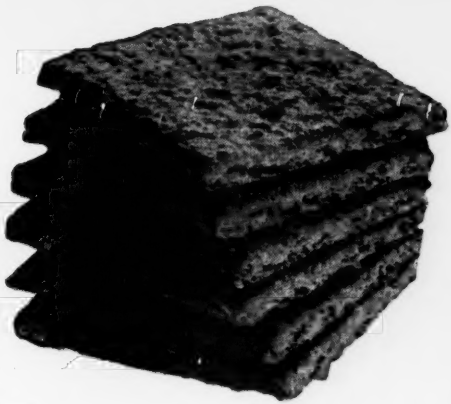

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DOSAGE: 1 or 2 MELOZETS Wafers ½-hour before meals or when hungry. *A full glass of water* must be taken with each wafer to insure proper bulk formation. Not more than 8 wafers should be taken in a 24-hour period. MELOZETS are contraindicated in the presence of intestinal obstruction. MELOZETS are packed in ½-lb. boxes, containing approximately 25 methylcellulose wafers.

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*Patent applied for

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FREDRICK F. YONKMAN, M.D.*
Columbia University, New York City

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THE sympathetic portion of the autonomic nervous system is frequently spoken of as the adrenergic division, a term implying that its stimulation results in manifestations of an adrenaline (epinephrine) type of activity.

A sympathomimetic agent is one that duplicates or mimics the dynamic influence of the sympathetic nervous control of an organ such as the iris, heart, stomach, or bladder. Such an agent is frequently referred to as an adrenergic stimulant, since generally it likewise duplicates the action that results from an injection of adrenaline; hence, the pupil dilates (adrenergic stimulation of the pupillary dilator muscular fibers of the iris), the heart rate increases, the stomach relaxes, the sphincter of the urinary bladder contracts, and so on.

An agent that blocks or interferes with the action of adrenaline or the effects of sympathetic nerve stimulation is known as an adrenergic blocking agent. Formerly such an agent was termed adrenolytic if it blocked the effects of adrenaline, sympatholytic if it blocked the effects of electrical stimulation of any sympathetic nerve at an end organ.

Strictly speaking, the terms adrenolytic or sympatholytic, although still used by some, are not accurately descriptive, since neither adrenaline nor sympathin (norepinephrine) is lysed or "washed out." In any event, once adrenergic blockade is established, adrenaline or sympathin is still present but cannot exert the full action on tissues or organs normally responsive to it.

In clinical practice there are numerous abnormal conditions which may call for varying degrees of adrenergic blockade. By proper selection from the various types of adrenergic blocking agents available today, the physician is in an excellent position to cope more readily with the numerous challenging conditions that are reflected in his patients as evidence of sympathetic predominance. Such conditions seem to be either due to or associated with some degree of vasospasm (arterial or venospasm or both) which may be a reflection

(Continued on page 150)

*Lecturer in Pharmacology and Therapeutics, Columbia University, College of Physicians and Surgeons, New York City.

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1. Moyer, J. H., and Handley, C. A.: Federation Proc. *11*:378, 1952.
2. Greiner, T.; Gold, H.; Warshaw, L.; Palumbo, F.; Weaver, J.; Mathes, S., and Marsh, R.: Federation Proc. *11*:352, 1952.
3. Goldman, B. R., and Steigmann, F.: J. Lab. & Clin. Med. *40*:803, 1952.

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   'Neo-Penil' has also been reported to give higher concentrations in: brain tissue, spinal fluid, umbilical cord blood, pleural and ascitic fluids, and in red and white cells, and may also concentrate in bone marrow, spleen and lymphoid tissue. Further work may demonstrate that 'Neo-Penil' is useful in treating bacterial infections in these tissues.

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'NEO-PENIL' is the new antibiotic agent—derived from penicillin—which gives higher concentrations in the lung and sputum.

References

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2. Flippin, H.F.: Chicago Session A.M.A., 1952.
3. Segal, M.S., and Dulfano, M.J.: GP 7:57 (Jan.) 1953.

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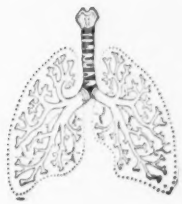


of overactivity of the sympathetic nervous system. These include:

Peripheral vascular disease
- Arteriosclerosis obliterans
- Diabetic gangrene
- Thromboangiitis obliterans
- Raynaud's syndrome
- Livedo reticularis
- Acrocyanosis
- Causalgias
- Trench and immersion foot
- Thrombophlebitis
- Acute ischemia (poliomyelitis)
- Lymphedema
- Posttraumatic edema
- Frostbite
- Scleroderma
- Endarteritis
- Herpes zoster
- Postherpetic neuralgias
- Popliteal aneurysm and embolism
- Dysmenorrhea

Hypertension

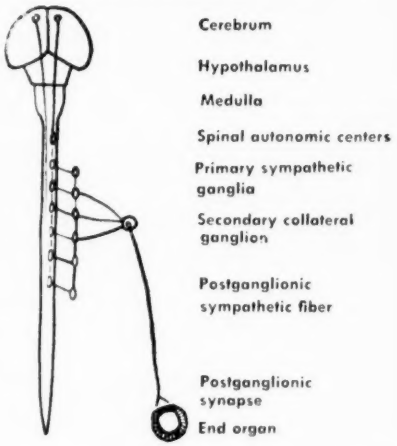
Cerebral accidents, thrombotic and vasospastic

One may speak of these disturbances as evidence of sympathetic or adrenergic predominance. The several areas of the central and peripheral nervous system which may act as foci of impulses responsible, for example, for the spasm of a blood vessel are shown in the illustration, which indicates several possible areas of attack in the attempt to block out such dominant or overactive sympathetic or adrenergic influence. The main areas are the hypothalamus and the upper medulla oblongata (probably), spinal autonomic centers, primary and secondary sympathetic ganglia, and peripheral arborizations of the sympathetic nerve fibers at their juncture in the blood vessel or in other sympathetically controlled end organs. Hence one speaks, in reverse order, of peripheral, ganglionic, and central blocking agents.

Peripheral Blocking Agents

One of the earliest known adrenergic blocking agents of the peripheral type is *yohimbine*. Its vasodilating properties exercised in the corpora cavernosa, possibly through its "antisympathetic" activity, no doubt earned for it the dubious reputation of an aphrodisiac. However, other central stimulating properties may well be responsible for this reputation, since currently used vasodilators of the adrenergic blocking type have not earned the aphrodisiac halo. Today, because of the marked side reactions associated with even subeffective clinical dosage, yohimbine enjoys little use as an agent of general applicability in the diseases tabulated above.

ANDRENERGIC CONTROL



Various members of the ergot family have been isolated but, until recently, only *ergotamine tartrate* (Gynergen) has been used clinically. Although its adrenergic block-

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ing capacity can be successfully employed for migraine of spastic origin, its chief use is for the congestive form, in which the fundamental and characteristic "ergot action" of smooth muscle stimulation is exercised. In this instance the dilated cranial blood vessel or vessels must be restored to normal caliber if the accompanying relief is to be properly interpreted, since the drug's adrenergic blocking action could only aggravate migraine of the congestive type.

More recently, members of the ergotoxine group of ergot alkaloids have been altered by the Sandoz chemists to produce *dihydroergocristine, dihydroergokryptine,* and *dihydroergocornine,* each a very potent adrenergic blocking agent. Dihydroergocornine has been reported upon the most frequently when any of the 3 compounds has been employed alone in peripheral vascular disease other than neurogenic hypertension. In the latter condition the 3 alkaloids are appropriately combined to form the preparation, *Hydergine,* which is effective orally as well as parenterally.

These alkaloids have not only strong adrenergic blocking action at the spastic blood vessels but also exert a central suppressive action which seems to prevent excessive outflow of sympathetic impulses, probably in the region of the brain stem. This action could well account for the desirable slowing of the heart rate which is so characteristic of this group of compounds.

The effects of one of these alkaloids in producing an adrenergic blockade may be observed as follows: An injection of adrenaline into the femoral artery produces a definite blanching of the foot. However, an injection of adrenaline given some thirty minutes after an injection of dihydroergocornine will produce no vasoconstriction, indicating a strong blockade effected by the ergot alkaloid.

Although no accurate statement can yet be made regarding the ultimate status of these compounds, sufficient information is available to indicate that they may continue to enjoy their favorable reputation, provided tolerance to their sustained action may be circumvented, especially in terms of antihypertensive therapy.

Dibenamine still remains nothing more than a scientific curiosity. Its absolute limitation to intravenous administration warranted an early impression that this compound would probably never be introduced for general use. This early impression has been sustained for, obviously, the general practitioner must be assured of safe medication. "Chemical cousins" of Dibenamine in the form of No. 688A and others offer more promise, however, and bear some watching, especially if the side reactions, such as severe tachycardia in many patients and gastric intolerance in others, can be conveniently overcome.

One of the earliest known antagonists of epinephrine is *histamine.* Whereas epinephrine tends to raise the blood pressure by constricting blood vessels, as they are constricted by sympathetic nerve stimulation, histamine in many areas tends to do the opposite. In other words,

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1. Riseman, J. E. F. and Brown, M. G. Arch. Int. Med. 60: 100, 1937
2. Brown, M. G. and Riseman, J. E. F. JAMA 109: 256, 1937.
3. Riseman, J. E. F. N. E. J. Med. 229: 670, 1943.

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epinephrine causes a hypertensive response, whereas histamine, in the normal subject, tends to decrease blood pressure, not necessarily by blocking sympathetic vasoconstrictor nerve impulses, but by relaxing the smaller arterioles directly as well as by increasing capillary permeability. Epinephrine results in blanching of skin vessels but histamine frequently causes a flushing of superficial areas.

Because of the numerous side reactions associated with histamine, many attempts were made to modify the histamine or imidazoline nucleus to prolong its activity and decrease its side reactions. One of the results was the chemical development of 2-benzyl imidazoline, known as *Priscoline*. Evidence of its vasodilating properties is shown by the flushing or reddening of the skin after intravenous, intramuscular, or oral administration. Skin temperature is also increased, especially in the fingers and toes, as has been demonstrated by Wakim, Peters, and Horton of the Mayo Clinic, a feature of practical import when considering the application of adrenergic blockade in the previously cited conditions associated with sympathetic predominance.

Among these conditions are 3 especially important ones in which adrenergic blockade may be successfully applied by proper choice of agents. These indications may bear special emphasis because of the nature and distribution of the conditions, as well as their importance in the public mind. Here again may we stress the fact that any effective adrenergic blocking agent, whether of the peripheral or ganglionic type, may produce some degree of the desired action.

Neurospastic Dysmenorrhea

Intractable neurospastic dysmenorrhea, for example, has been successfully treated by the combined use of Priscoline and nicotinic acid, both vasodilating agents. The latter produces vasodilatation by direct action upon the smooth muscle of the blood vessel, and the former by dual actions—a direct histaminic or nitrite-like action on the smooth muscle of the blood vessel and a peripheral adrenergic blocking action against the vessel's sympathetic nerve control.

Griffith and Little found that Priscoline given orally was effective, but that better results were obtained when the administration was accompanied by intravenous injections of nicotinic acid. These authors offer an intriguing explanation of their gratifying results. They believe that the uterine vessels, particularly the arterioles, contain sensory dendrons which, when impinged upon or compressed under the influence of sympathetic predominance, give rise to painful stimuli of varying intensity and that under the influence of any type of vasodilator, as employed in their investigation, they have produced, in effect, a decompression of the excited sensory painful dendrons in the blood vessel walls.

Poliomyelitis

Another interesting use for adrenergic blocking agents is to relieve pain in the acute, painful, and

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because it usually "can be given intermittently for long periods without toxicity and at relatively low cost."[1]

"Of importance because of its frequent occurrence and refractoriness to all antibiotics is chronic non-specific prostatitis."[2]

The danger of toxic reactions may preclude administration of sulfonamides to patients who require protracted therapy.

1. Hinman, F., Jr.: California Med. 7:1 (Jan.) 1952.
2. Furlong, J. H.: Delaware State M. J. 24:170, 1952.

Recommended therapeutic dosage: 3 to 4 tablets t.i.d.

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distressing phases of poliomyelitis which, according to Smith and associates, may well be due to involvement of the sympathetic ganglia and of the lateral horn of the spinal cord. These well-known damaging effects of the poliomyelitis virus on the cell bodies of the anterior horns are apparently carried over to the sympathetic neurons to some degree and especially to the sympathetic ganglia in certain regions. The "irritating" effects of the virus in the sympathetic chain could manifest themselves in painful vasospasm of certain blood vessels in either superficial or deep areas of the limbs and elsewhere.

Smith reasoned that prolonged treatment with a relatively safe, easily administered drug might produce benefits similar to those afforded by the hot-pack treatment of Sister Kenny. The report of Smith and associates, which covers some 600 patients treated at the Kingston Avenue Hospital in Brooklyn, indicates that Priscoline seemed to be of definite but varying value in approximately 75% of the cases. Smith's results have been corroborated by many investigators; the conclusions of Polley of the St. Louis University Hospital summarize very well the favorable effects obtained:

1. Fever was not considered a contraindication for the use of Priscoline. However, a greater tendency toward nausea was noted among the febrile patients.
2. In general no toxic effects were noted. The appearance of a "flush" and the occurrence of nausea were expected and did appear. Patients behaving in this manner were continued on the drug but at a reduced dosage. Eliciting a flush did not seem to increase the efficiency of the therapeutic response.
3. It was the opinion of those who had observed the operation of the same division during previous years that the results achieved with Priscoline were equal to the results obtained when the hot pack methods had been closely followed. It was a pleasant experience to find an efficient substitute for the time-consuming and cumbersome hot pack equipment.

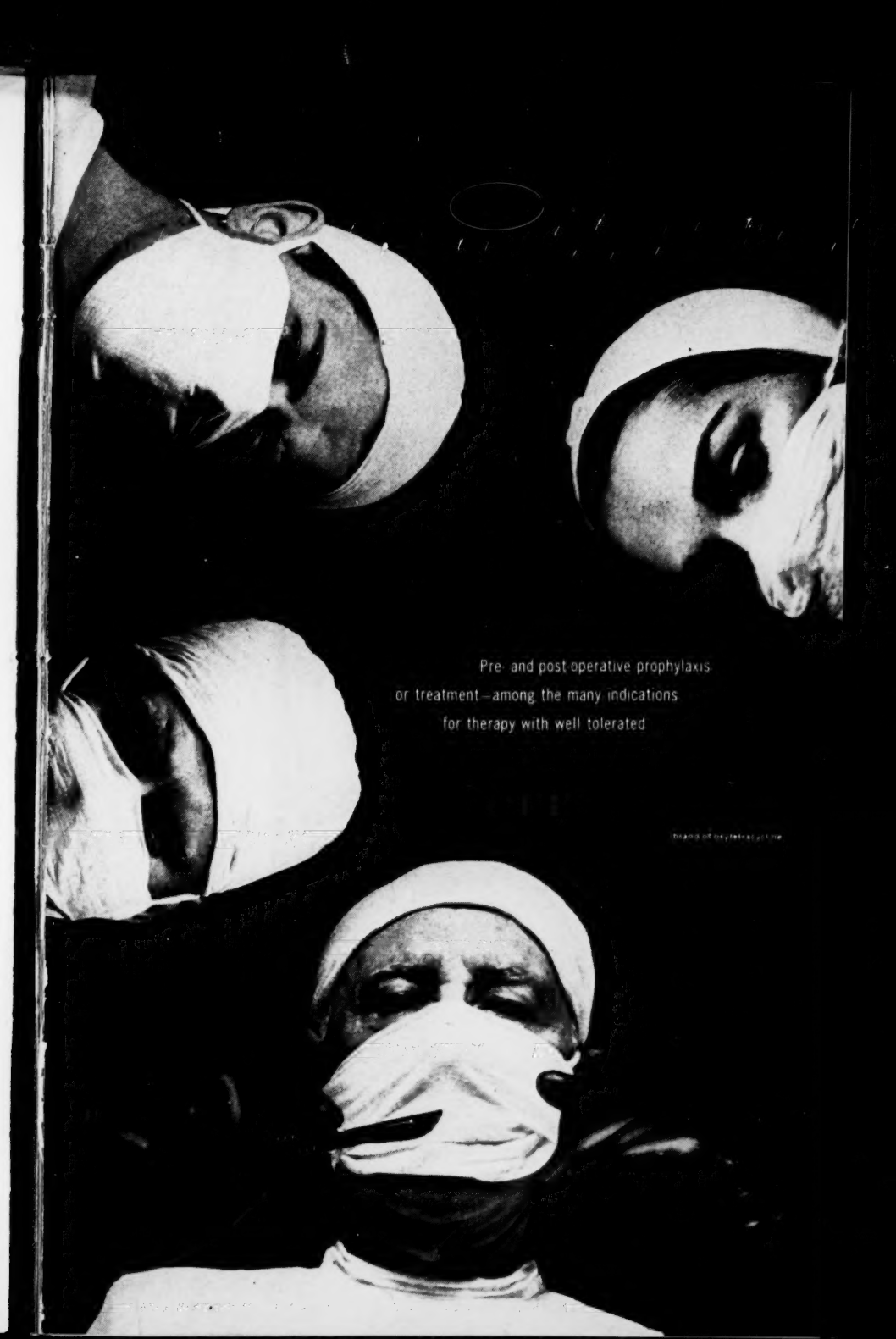
Any effective adrenergic blocking agent used either by itself or in conjunction with a safe drug which dilates the vessels directly without significantly decreasing blood pressure may produce equally favorable results.

Cerebral Accidents

Acute cerebral accidents, so often encountered by the general practitioner, are of special import with reference to adrenergic blocking activities. Whether due to hemorrhage or thrombosis, such accidents may well have an associated element of vasospasm. This vasospasm is undoubtedly of a secondary or reflex nature associated with hemorrhage or thrombosis, but the end result would be similar to that which is associated with primary vasospasm unaccompanied by either hemorrhage or thrombosis. In any event there is definite proof that sympathetic predominance to the point of producing vasospasm frequently, if not invariably, prevails in all such cerebral vascular accidents.

In such a condition, sympathectomy or stellate ganglionic blockade with novocain may be effec-

(Continued on page 160)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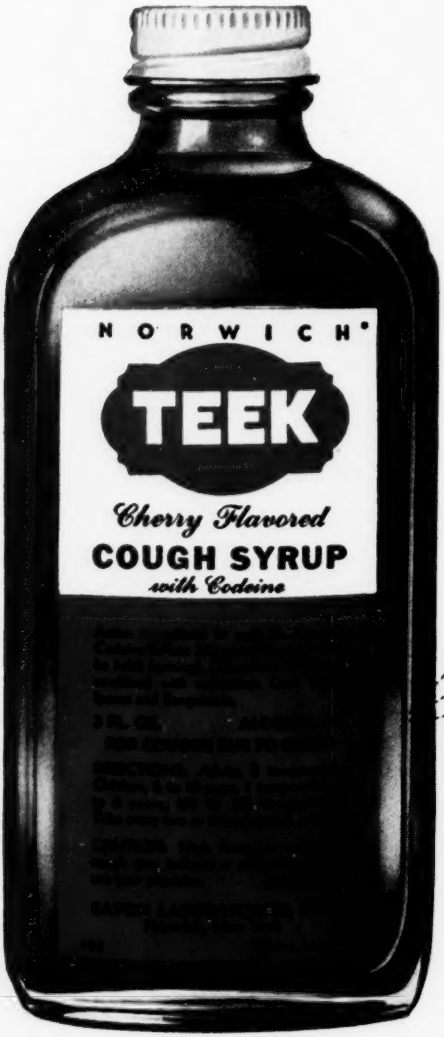

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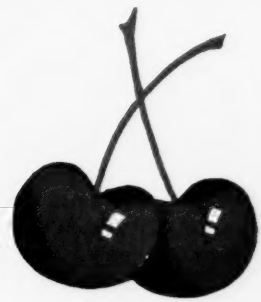

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tive, but Etamon or Priscoline may produce similar beneficial results by relieving the vasospasm of the affected cerebral vessels. Thus Prandoni and Alpert have employed 3 to 6 mg. of Priscoline, intracarotidly, on the affected side, with almost immediate beneficial results. Similar favorable effects were achieved by Bennett after intravenous administration of 1.5 cc. (37.5 mg.) of Priscoline for a man in his early 70's who had just suffered a cerebral vascular accident. The patient in the past three years had had a coronary thrombosis as well as 2 previous cerebral episodes of thrombosis. Within two minutes after the injection the facial paralysis disappeared, the patient was able to say a few words and move the arm and leg that had been previously almost completely paralyzed. The man was given novocain stellate ganglion block two hours afterward and later had 4 others. He was also given Dicumarol by mouth.

Except for some remaining difficulty in his speech, the patient made an excellent recovery.

It is conceivable that adrenergic blocking agents of this type may also be effective as oral therapy in certain types of cases. This seems to have been well corroborated by VandenBerg:

> I have had an increasing number of cerebrovascular disorders which have apparently benefited from oral and parenteral Priscoline. This has been especially gratifying in hypertensive encephalopathies and as prophylaxis during prodromal paresthesias which so frequently precede actual cerebral thrombosis.

Again it should be emphasized that in this condition, as well as in the others classified as peripheral vascular diseases, any effective vasodilator of the adrenergic blocking type may be potentially valuable, provided an undesirable fall in blood pressure is not produced.

Side Reactions

As with the administration of all valuable drugs, various types and intensities of side reactions may well appear. With clinically effective doses of Priscoline a flushing of the skin and goose flesh, as well as a feeling of chilliness, sometimes occur. Usually these reactions are not sufficiently disturbing to necessitate discontinuance of therapy. More disturbing, although less frequent, and usually appearing only after higher doses than ordinarily required, are the symptoms of nausea, postural dizziness, apprehension, and, occasionally, vomiting, as well as audible peristalsis and sweating. Headache or stuffy nose may also occur, the latter probably indicating that complete adrenergic blockade has been effected in the nasal area.

Most patients grow accustomed to the milder side reactions of the agent and some become adjusted even to the nausea and gastrointestinal distress. If the latter are particularly annoying, they can sometimes be obviated by reducing the dosage or by adding a vagal blocking agent, such as atropine, belladonna, or one of the synthetic agents, such as Banthine, Pavatrine, Syntropan, Trasentine, or Antrenyl. If adequate relief is not

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obtained by such antagonistic therapy, the drug must be withdrawn and the patient given a compound like Roniacol which may not always be as effective in treating the peripheral vascular disease but is usually well tolerated as far as gastrointestinal distress is concerned.

Recently other more important side reactions to Priscoline have become apparent. These appear as gastric hypersecretion to the point of exacerbation of the symptoms of peptic ulcer, exacerbation of coronary insufficiency in some patients, and hyperinsulinism in diabetes mellitus.

Gastric hypersecretion can usually be controlled either by reduction of dosage or by the addition of an appropriate antacid regime. It is probable that such hypersecretion may well be associated with the imidazoline or histaminic nature of the compound.

Exacerbation of coronary insufficiency must be borne in mind, particularly in elderly patients with cardiac histories. Such results may be due to either [1] a redistribution of available blood supply into dilated areas (splanchnic?) away from an already embarrassed myocardium or [2] a direct cardiotonic effect of Priscoline as evidenced by palpitation and increased cardiac output. It is well to employ small test doses to determine how well the cardiac patient tolerates the drug.

There have been reports of some approximately 20 or 30 diabetic patients in whom symptoms of hyperinsulinism developed to a degree that the insulin requirements had to be reduced and at least readjusted.

This is not necessarily a serious complication but should be definitely remembered so that embarrassing or disturbing consequences may be obviated.

Regitine is a blocking agent of a comparable type but with less of the direct histaminic blood vessel relaxing property. On the other hand, Regitine is a stronger sympathetic blocking agent, comparable to Dibenamine and the dihydrogenated ergot preparations described above. It can be administered orally and can be substituted for Priscoline and similar medications which may not be well tolerated in certain patients. On the other hand, the appearance of tachycardia, particularly with increased dosage, may be more frequent. Other peripheral blocking agents are being studied and their release for general use may be anticipated before too long.

Ganglion-blocking Agents

Ganglionic blocking agents differ from peripheral blocking agents in that they interfere with the passage of sympathetic impulses at the sympathetic ganglia rather than at the ends of the nerve associated with blood vessels or other end organs. The first ganglionic blocking agent to be successfully employed in this country was *tetraethylammonium bromide* (Etamon).

Etamon has proved effective in all the vasospastic conditions cited above but, unfortunately, sustained use of the drug is somewhat limited because it can generally be giv-

en intravenously only. The high dosages usually required do not permit intramuscular, subcutaneous, or oral administration because of the hypertonic and irritating effects of the drug on the subcutaneous tissues and on the gastric mucosa, respectively. Other side reactions of importance in some patients include dryness of the mouth, dysphagia, and atony of the gastrointestinal tract and bladder, all associated with the generalized ganglionic blocking activity of this drug.

In other words, Etamon and other ganglionic blocking agents of that type are not specific in action, but block the parasympathetic ganglia as well as the sympathetic ganglia, thus resulting in atony or flaccidity of the gastrointestinal tract and the urinary bladder. Favorable effects are produced by establishing sympathetic ganglionic blockade, as in Buerger's disease.

More recently hexamethonium—known also as C_6, Bistrium, Methium, or Esomid—and other agents of different chemical structure known as Arfonad and Pendiomide have been prepared as substitutes for Etamon. All these ganglionic blocking agents act in the same manner but in varying degrees. They must be used with caution, not only because of their capacities to produce orthostatic hypotension of severe degree but also because of the variable rates of absorption from the gastrointestinal tract. If one could be assured that an oral dose would uniformly elicit a definite degree of response, this type of drug would be much more valuable.

Too often a ganglionic blocking agent is limited to intravenous, subcutaneous, or intramuscular routes of administration with obvious attendant disadvantages. Because of their profound capacity to produce ganglionic blockade and thereby establish a "medical sympathectomy" of the sympathetic nervous system, they are of definite but limited value in the treatment of essential and neurogenic hypertension. Here, too, if their sympathetic ganglionic blocking activities could be more or less restricted to the sympathetic ganglia with no blocking carryover to the parasympathetic portion of the autonomic nervous system, these drugs would be more valuable as adrenergic blocking agents.

Pheochromocytoma Diagnosis

From a diagnostic point of view, adrenergic blocking agents are valuable in certain clinical conditions but, in particular, in hypertensive patients for detection of a pheochromocytoma, a hyperfunctioning "tumor" of the medullary portion of the adrenal gland. If one were to use the histamine provocative test for such detection, hazardous hypertensive levels could be obtained which might be sufficiently dangerous to necessitate use of an adrenergic blocking agent.

Although histamine provocation is still employed by many, there is a strong tendency to use adrenergic blocking agents which may result in hypotension rather than

(Continued on page 166)

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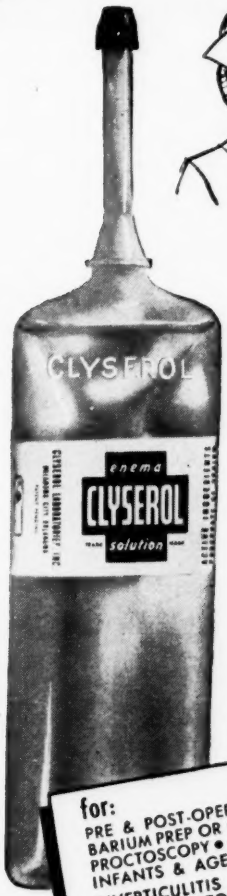

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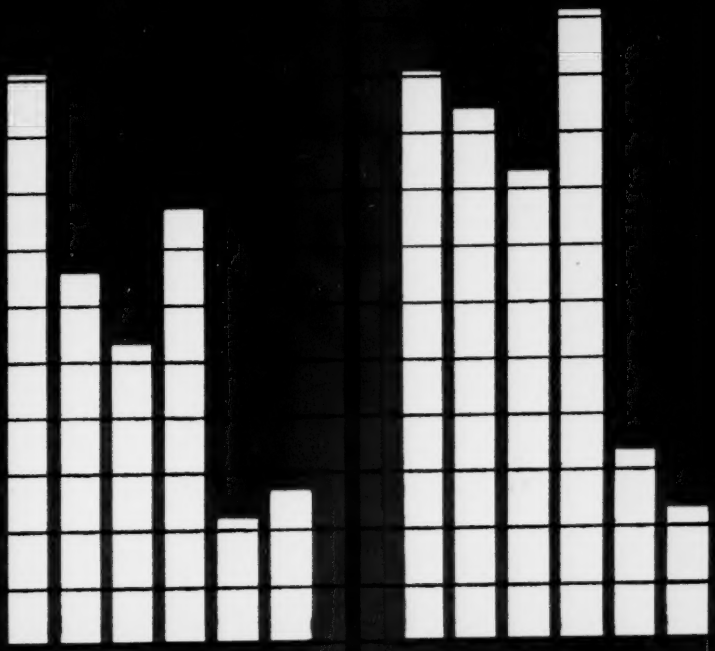

in histamine-induced hypertension.

Thus one sees several comparable agents employed. All have been used successfully intravenously but Grimson, in particular, stresses the fact that Regitine can be employed in small, 5-mg., dosages *intramuscularly*, this dose to be repeated intramuscularly within fifteen minutes if necessary. These injections usually result in a significant fall in blood pressure if the patient harbors a pheochromocytoma but "false positive" reactions may be encountered in the presence of uremia or barbiturate sedation!

Such a simple technic, which permits the use of a well-tolerated, effective drug in small dosage, makes available to the general practitioner a ready means whereby he may be the first outpost in "screening" a patient with pheochromocytoma, a lesion whose associated hypertension is the form most consistently amenable to surgical treatment.

Furthermore, in preparation of this type of hypertensive patient for surgery, either intravenous, intramuscular, or oral treatment with Regitine may be employed.

With the general use of well-tolerated agents of this type, especially those which can be given by the intramuscular route to all hypertensive patients, there would seem to be little doubt that the detection of pheochromocytomas by the general practitioner should definitely increase, along with the extreme gratification afforded him by success in such Sherlock Holmes proclivities. His endeavors, as well as those of the expert surgeon to whom the patient is referred, will be lifesaving for many patients.

Hypertension Therapy

In the field of essential or neurogenic hypertension, adrenergic blocking agents may be of definite value. This is especially true of Hydergine, Etamon, hexamethonium, and, more recently, Apresoline. Some of these are ganglionic blocking agents as previously indicated and others are peripheral blocking agents in the sense of antagonizing epinephrine and norepinephrine.

Apresoline is weakly antiadrenergic in its capacity to antagonize the vasoconstrictor effect of epinephrine and norepinephrine, but this effect becomes more pronounced as the dosage of the compound is increased. Of more importance perhaps is the capacity of the agent to suppress or to antagonize the vasoconstrictor effects of serotonin, pherentasin, and, to some extent, angiotonin, all of which have been indicted as responsible for or associated with the production of hypertension, especially of the neurogenic and renal types.

It is thought by Taylor, Page, and Corcoran of the Cleveland Clinic that serotonin or a serotonin-like substance may be produced in the brain and thus result in sustained hypertension; it is likewise thought by Schroeder of Washington University that pherentasin, which is found in arterial blood of certain hypertensive patients, may be chiefly responsible

(Continued on page 170)

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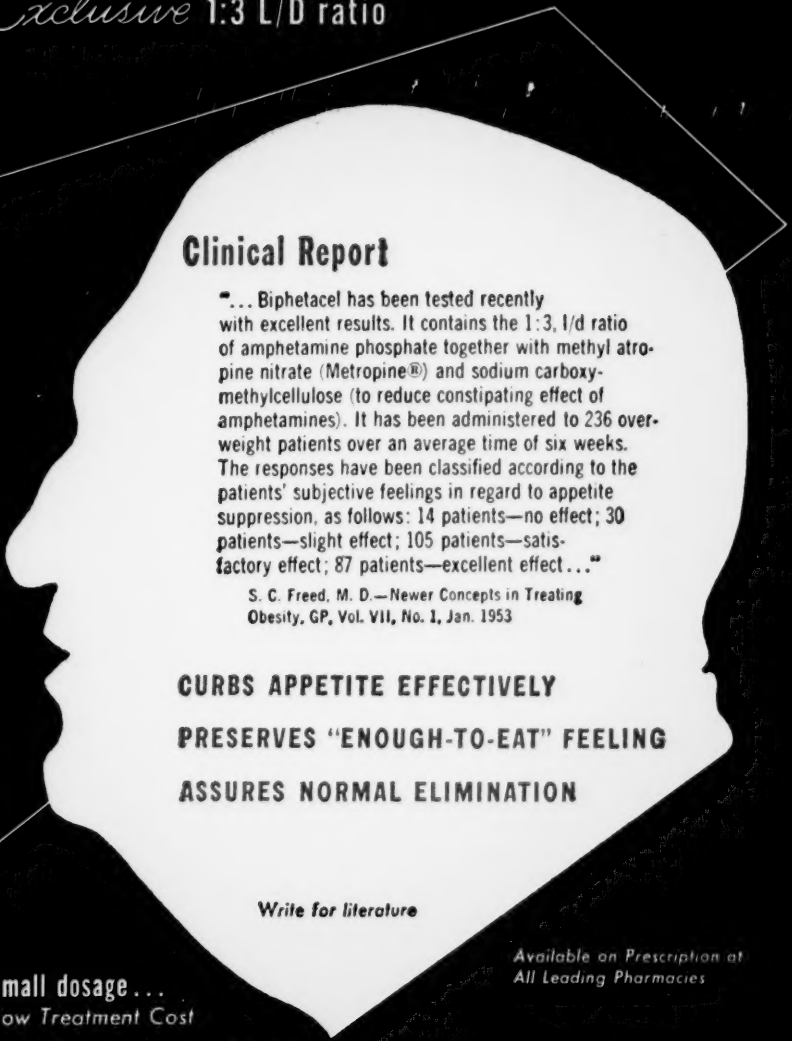

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S. C. Freed, M. D.—Newer Concepts in Treating Obesity, GP, Vol. VII, No. 1, Jan. 1953

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for the development and maintenance of their hypertension. Both these agents are vasoconstrictors as indicated and thus produce elevated blood pressure. Whether they can be produced by the stimulation of a sympathetic nerve is apparently not known at this time, so it cannot be said with certainty that they actually act like epinephrine and norepinephrine, but it can be stated that they duplicate the effects of these vasoexcitors. In this sense they can almost be considered to be sympathomimetic since they mimic to some extent the effects of sympathetic neurostimulation. Of special interest, however, is the fact that Apresoline can antagonize the effects of both serotonin and pherentasin and, in this sense, could be called an antisympathomimetic agent if not a true adrenergic blocking agent.

As an antisympathomimetic agent, Apresoline desirably decreases cerebral vascular tone as well as renal vascular resistance, both blocking effects being highly valuable in any type of hypertension, the former in hypertensive encephalopathy and the latter especially in that hypertension associated with the toxemia of pregnancy and acute glomerular nephritis. For patients classified as "sympathectomy failures," the compound is thus of special interest because of its favorable action in reducing blood pressure in such cases.

Such failures may well be due to a humoral component not affected by sympathectomy. Could such humoral substances be serotonin, pherentasin, and similar agents? It would seem plausible on the basis of their known antagonism as exercised by Apresoline. On the other hand, it would seem that in certain hypertensive patients, stronger neural blocking agents such as peripheral and ganglionic blocking agents might be required to block the strong prevailing sympathetic component.

As an antisympathomimetic agent, Apresoline elicits certain side reactions, chief of which is headache; this is apparently of the congestive migraine type, comparable to the condition resulting from loss of vasoconstrictor control. It seems, however, that headache from the compound is not due to adrenergic blockade but to the release of histamine after large doses of the agent, since this drug inhibits the action of histaminase, the enzyme responsible for the destruction of histamine. It is also known that this histaminic type of headache can be prevented by antihistaminic agents but better still by initiating therapy with very small doses of Apresoline, 5 or 10 mg., four times a day.

Conclusion

By proper selection from the various types of adrenergic blocking agents available today, the physician is in excellent position to cope more readily with the numerous challenging problems that are reflected in his patients as evidence of sympathetic predominance.

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Medical Forum

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Early Cancer of the Uterus*

QUESTION: Is vaginal hysterectomy advisable after the menopause for benign disease of the genital organs as prophylaxis against cancer?

Comment invited from
A. N. Arneson, M.D.
J. Ernest Ayre, M.D.
J. Robert Willson, M.D.
Mitchell J. Nechtow, M.D.

► TO THE EDITORS: A review of the interesting report by Drs. Olin S. Cofer and Albert L. Evans seems to raise immediately two pertinent questions. The first concerns improved support that may be attained by removal of the uterus when vaginal plastic operations are indicated. That is an elective procedure and solved best upon the basis of requirements for the individual patient.

The second question is in reference to cancer prevention. The value of vaginal hysterectomy in cancer prevention might be expressed as the ratio of expected cervical cancer rate less the expected cure rate versus the mortality from vaginal hysterectomy. A similar question has long been debated in considering total hysterectomy versus subtotal hysterectomy. In the latter instance there is little doubt that total hysterectomy is preferred. In the case of vaginal hysterectomy the cervix is removed. The value of that procedure in preventing cancer must, however, remain debatable.

Such an extension of operation in plastic repair, when vaginal hysterectomy is applied almost routinely in elderly patients, represents something of a departure from our usual more conservative attitudes. The authors mention the importance of preserving the ovaries. If the operative procedure is applied as a means of preventing cancer it would seem that the operation should include also removal of the ovaries to avoid development of malignant tumors in those structures.

One final point might be made. Among 746 vaginal hysterectomies the authors found 30 cases of unsuspected early cancer of the cervix. During the observation of 744 of the patients treated surgically only 1 has shown evidence of recurrence. It is surely not the intention of the authors to advocate vaginal hysterectomy as a means for detecting cervical cancer which can be accomplished more simply by means of smears and adequate bi-

*MODERN MEDICINE, Oct. 15, 1952, p. 104.

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opsy with exploration of the cervical canal. More detailed preoperative diagnosis is of inestimable value.

For lesions localized within the epithelium itself, simple hysterectomy has been demonstrated to be effective treatment. With true invasive cancer the possibility of dispersion exists.

One of the important pitfalls in the treatment of suspected intraepithelial cancer has been the subsequent detection of true invasion after the uterus was removed. It would seem, therefore, that that consideration should be given more careful preoperative diagnosis and, after exploring the cervical canal and following other procedures for the detection of true invasion, some segregation of patients might be made so that those with invasive cancer would as a group be treated more adequately.

A. N. ARNESON, M.D.
St. Louis

► TO THE EDITORS: In my opinion, vaginal hysterectomy is advisable after the menopause for benign disease of the genital organs if and when such disease calls for major surgery.

I am fully aware that one school of gynecologists has recommended removal of the nonfunctional uterus after the menopause in order to insure that no cancer will develop in those tissues. In the light of present-day advances in methods of detection of early cancer of the uterus, it is my conviction that such a radical approach is not justified.

Over 90% of genital cancer arises in the uterus and the point of special predilection is the uterine cervix. Cervical cytology has attained a remarkable degree of accuracy and efficiency in detecting cancer. Indeed, preclinical cancer may be detected as long as seven years before the lesion becomes obvious. Therefore, the postmenopausal female may secure remarkable protection against this form of cancer by having a cervical cell smear or cell scraping every one to two years. This will detect cervical cancer at an extremely early stage while readily curable and will also detect cancer of the body of uterus with a considerable, though lesser, degree of accuracy. The cervical smear will also detect the rarer cancer of the fallopian tube earlier than other methods.

This leaves the difficult question of ovarian carcinoma and its detection untouched. However, if women can be educated to have an annual cervical cytology test and pelvic examination, which is an integral part of any cancer detection examination, even cancer of the ovary may be found in a more favorable stage.

Vaginal hysterectomy is a splendid operation in the hands of those trained in its technics. It was recently my privilege to see Prof. Bastiannse in Amsterdam perform the Schauta vaginal hysterectomy for cancer of the cervix. The very good results achieved by such an expert point to a useful place for this procedure in the hands of one specially trained. However, that is cancer therapy and I cannot con-

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Acting rapidly in a significantly high percentage of patients, the parenteral solutions of Veriloid afford a positive means of reducing critically elevated blood pressure. They have been found of great value for the relief of the distressing symptoms of prolonged, severe blood pressure elevation, and in hypertensive emergencies when the degree of hypertension assumes life-threatening proportions. These parenteral hypotensive agents are indicated in hypertensive states accompanying cerebral vascular disease, malignant hypertension, hypertensive crisis (encephalopathy), toxemias of pregnancy, pre-eclampsia, and eclampsia.

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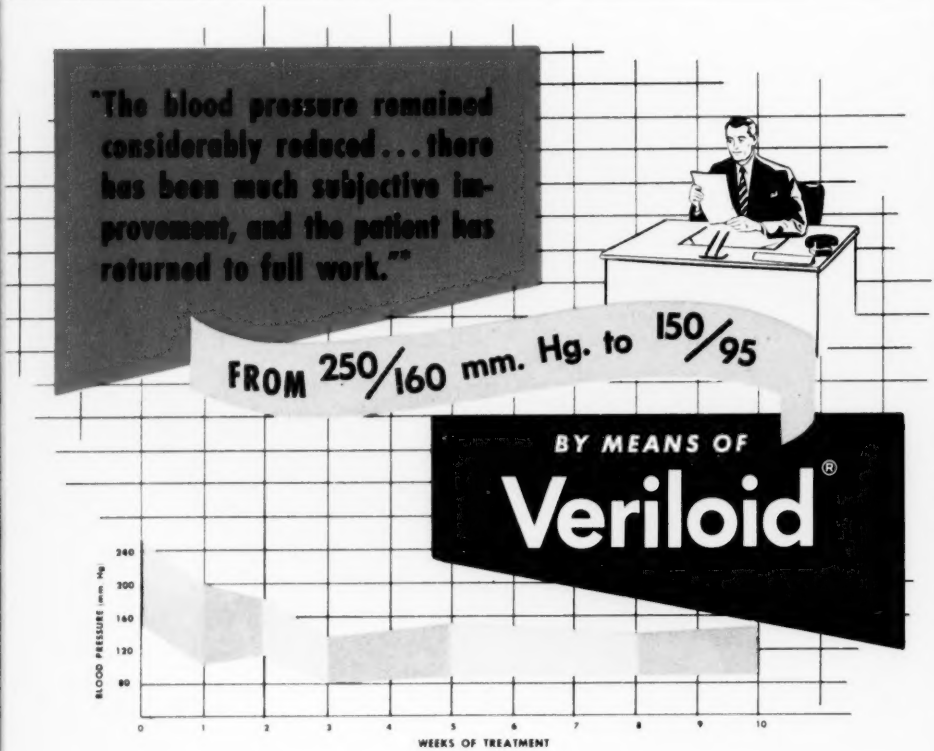

Veriloid is available in three dosage forms:

Veriloid (plain) in 1, 2, and 3 mg. scored tablets; starting dosage 9 to 15 mg. daily, to be adjusted according to response and tolerance.

Veriloid with Phenobarbital (Veriloid-VP), each scored tablet presenting Veriloid 2 mg. and phenobarbital 15 mg.

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This male patient, 41 years of age, was given the same dose of Veriloid tablets (26 mg. daily) for a period of five months. During that time, he was able to resume his normal sedentary occupation at full activity. Note the prompt and sustained reduction in diastolic pressure and the subsequent good reduction in systolic pressure.

Not every patient shows this spectacular response to oral Veriloid. However, a sufficiently large number do, warranting the administration of this hypotensive agent to every patient with elevation of blood pressure sufficient to require treatment.

*Kauntze, R., and Trounce, J.: Treatment of Arterial Hypertension with Veriloid, Lancet 2:1002 (Dec. 1) 1951.

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ceive any justification in applying *radical surgery* purely for prophylaxis when more effective detection methods may be applied simply and without surgical risk.

J. ERNEST AYRE, M.D.
Miami

► TO THE EDITORS: While it is true that removal of the uterus for conditions such as cervicitis and in conjunction with vaginal plastic procedures, as suggested by Drs. Cofer and Evans, will prevent the subsequent development of uterine cancer, the proposed procedure has little merit. The common lesions of the cervix can be eradicated by measures far less dangerous than hysterectomy with which, in the best clinics, there is a small but inevitable mortality. Since hysterectomy does little to improve the end results of the usual vaginal plastic procedures, it is unnecessary except in some cases of uterine prolapse.

Early malignancies found by examination of the removed uteri in this study could undoubtedly have been detected by careful preoperative examination, in which event treatment more appropriate than total hysterectomy could have been instituted. Although surgical therapy is indicated for certain patients with uterine cancer, pretreatment knowledge of the type and extent of the lesion is necessary so that the treatment most suitable for the malignancy can be planned.

Periodic complete prophylactic physical examination of presumably well women will afford an opportunity for the detection, not only of genital tract cancer in its earliest stages, but also of both malignant and benign conditions in other parts of the body. This should provide the best total care for the individual. If the authors' suggestions are generally applied throughout the country I wouldn't be surprised if the mortality from this "prophylactic" procedure exceeded that from the cancers which might be prevented by the removal of the uterus.

J. ROBERT WILLSON, M.D.
Philadelphia

► TO THE EDITORS: It has been the practice of Dr. Walter J. Reich and myself at the Cook County Hospital Gynecologic Clinic and in private practice to establish a preoperative diagnosis regarding the presence or absence of malignancies of the cervix and the endometrium before any surgical procedure is carried out. The Papanicolaou smears, multiple punch biopsies, and dilatation and curettage are used for such diagnosis.

If a benign condition of the cervix is found, it is managed by thorough electrocauterization. Simple cystoceles and rectoceles without any clinical symptomatology are not operative unless they reach large proportions. For prolapse in a patient who has reached the menopause, vaginal hysterectomy with plastic repair is employed.

We do not, prophylactically, resort to surgery unless indications for intervention are definite.

MITCHELL J. NECHTOW, M.D.
Chicago

Do Antibiotics Cause Fungus Infection?*

QUESTION: Has free use of antibiotics increased incidence of fungus infections of mouth, gastrointestinal tract, skin, or vagina?

Comment invited from
William H. Harris, Jr., M.D.
Perrin H. Long, M.D.
Henry Brainerd, M.D.

► TO THE EDITORS: Dr. Albert M. Kligman's paper is timely and thought provoking. He presents evidence that fungus infections have not increased as a result of the extensive exhibition of antibiotics. From my own clinical experience as well as that of my colleagues in a group practice consisting largely of adult patients, a similar impression has been gained. Moniliasis has been reported as a rather common complication of broad-spectrum therapy, but fortunately we have not observed mucous membrane involvement of the mouth or vagina by this fungus sufficiently often to curtail our use of these valuable agents.

Dr. Kligman points out that the mere isolation of *Candida albicans* is not enough for clinical diagnosis, thus making pulmonary and gastrointestinal involvement very difficult to prove. Since our administration of these antibiotics has been confined to systemic employment, we are not in a position to comment on untoward effects of application to skin surfaces. A pseudomembranous colitis developing during wide-spectrum therapy is probably not of fungal or bacterial origin. Studies to determine a causative agent have been unsuccessful so far.

WILLIAM H. HARRIS, JR., M.D.
Richmond, Va.

► TO THE EDITORS: There has been some increase in fungus infections since the wide-spectrum antibiotics have been used. However, in our experience, the infections have been quickly controlled and are not as resistant as normally occurring fungus infections. This is especially true of those of the skin and mucous membranes.

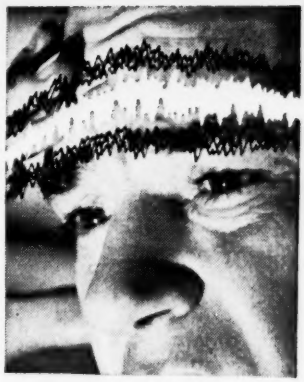
PERRIN H. LONG, M.D.
New York City

► TO THE EDITORS: Indiscriminate antibiotic therapy has increased very strikingly the incidence of superinfection with resistant forms of bacteria and yeasts. This is presumed to be due to suppression of the normal antibiotic-sensitive flora of the oropharynx and gastrointestinal tract, as well as of the genital tract in the female. As a rule, such infections are an unpleasant nuisance, but severe superinfection may occur with disastrous results.

It is doubtful that monilial infections of the mouth and genital area occur frequently in the absence of an irritative or sensitivity reaction to the drug. A patient manifesting such a reaction on one occasion will, as a rule, develop a similar reaction within a few hours of readministration of the drug at

(Continued on page 182)

*MODERN MEDICINE, Nov. 15, 1952, p. 130.



WHAT DOES pain SMELL LIKE, DOCTOR?

Waiting in the doctor's reception room can be quite a trial to some folks—laymen often associate pain with the odors of medication and antiseptics. And this can result in nervousness and tension.

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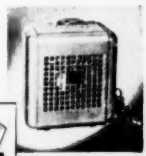

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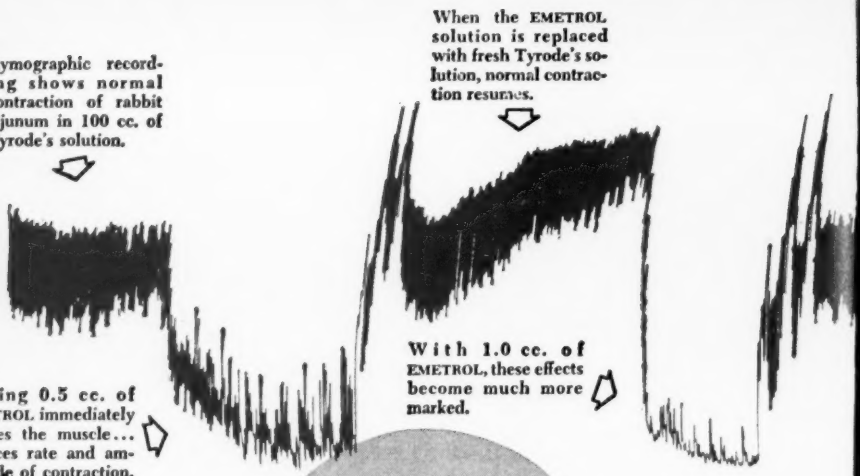

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EMETROL Phosphorated Carbohydrate Solution permits effective physiologic control of functional nausea and vomiting—without recourse to antihistaminics, sedatives, or hypnotic drugs.

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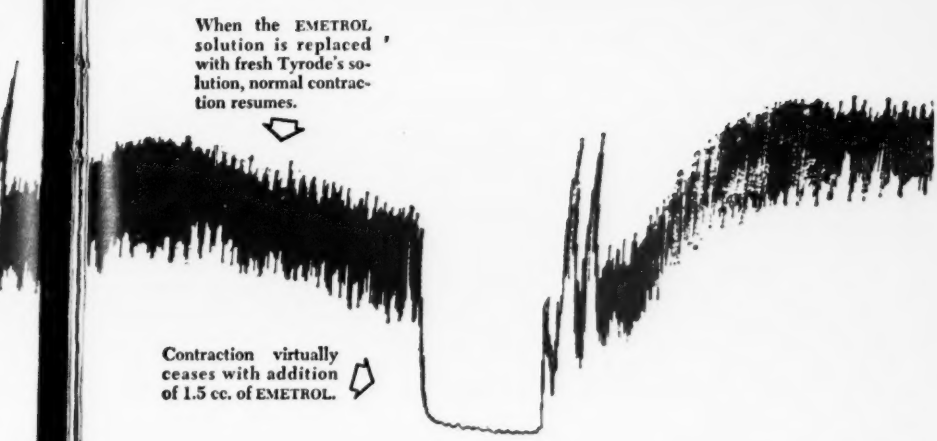

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a later date. Thus, drug sensitivity appears to play the primary role.

I feel that this problem of superinfection with resistant microorganisms is the most potent argument against the indiscriminate use of chemotherapy.

HENRY BRAINERD, M.D.
San Francisco

Internal Podalic Version and Extraction*

QUESTION: When is internal podalic version and extraction advisable?

Comment invited from
Charles S. Stevenson, M.D.
Philip H. Arnot, M.D.
Charles M. Steer, M.D.
Eugene S. Auer, M.D.
Charles P. McCartney, M.D.
William E. Gibson, M.D.
William F. Mengert, M.D.

► TO THE EDITORS: The article by Drs. William C. Keettel and Frank W. Crealock on internal version and extraction is another sound and practical paper from the Iowa group. Our experience here at the Herman Kiefer Hospital in the past five years has been similar in that we use the method only about once in every 1,000 deliveries.

The only situations in which version and extraction for delivery of a single pregnancy is indicated are [1] transverse presentation of the fetus, [2] rupture of the membranes, [3] prolapse of an arm, elbow, or scapula, and [4] full dilation of the cervix. If the cervix is not fully dilated but the patient is in good progressive labor, version and extraction is done only when full cervical dilation is achieved.

We first give ether anesthesia into the third stage, and then proceed with the maneuver, stressing slow and gentle turning of the fetus, using one hand internally and the other externally. An unscrubbed assistant, particularly one well experienced in the performance of external version, is of inestimable value to the scrubbed accoucheur and adds a great safety factor.

It is our teaching—along the line of preventive medicine—that careful palpation of the pregnant uterus should be done at every weekly prenatal office visit from the twenty-eighth to thirtieth week on, so malpresentation of the fetus can be detected early and corrected by external version as many times as necessary (*Am. J. Obst. & Gynec.* 62:488, 1951). In this way one is able to prevent a major portion of the natural instances of transverse presentation persisting until, and subsequent to, the onset of labor. Such practice will greatly decrease the number of transverse presentations in advanced labor which must be delivered either by cesarean section or internal podalic version.

I believe that the risk to the mother's life when internal version is performed is at least 50 times that of cesarean section in the hands of the average physician doing obstetrics. This general impression has been gained, at least in part, from sitting on the Mater-

(Continued on page 186)

*Modern Medicine, Nov. 1, 1952, p. 95.

When Chronic Fatigue, Insomnia are due to Low Blood Sugar Level...

Prescribing a simple change in diet may often restore energy and zest for living in many patients.

THE pace of modern living . . . business pressures, strenuous social activities, hurried meals, improper diet . . . all too frequently lead to exhaustion, loss of energy, inability to sleep. Now clinical studies show that these clinical manifestations are often associated with hyperinsulinism—causing a lowered *blood sugar level.**

Portis reported these fatigue states were aggravated when the patients consumed beverages and foods that contained free sugar. He further stated that while these raise the blood sugar level momentarily, their "free" sugar is burned up too quickly, and a greater letdown follows. On the basis of this evidence a diet high in proteins and relatively high in carbohydrates in a complex form was given to his patients. He found such foods as milk are especially beneficial because they are digested more slowly, and because they maintained the blood sugar level for a longer period.

For these reasons milk with Postum is suggested as a between-meal feeding and bedtime drink. It can often be of practical benefit to the patient. The milk provides nourishment that is slowly, steadily converted to blood sugar. Postum offers a pleasant and palatable flavor. Postum offsets the distaste for hot milk.

Moreover, Postum in the milk drink has a psychological advantage because many patients resent the taking of milk in itself as a regression to their childhood patterns. Postum has been recommended by doctors for over 40 years. It is widely known to your patients as a caffein-free drink—a beverage that has helped countless caffein-susceptibles to break the coffee and tea habit.

We will be glad to secure for you a reprint of Dr. Portis' article. We will also send you without charge a supply of Postum for your patients if you send in the coupon below.

*Portis, Sidney A., Life Situations, Emotions and Hyperinsulinism, J.A.M.A. **142:** 1281-1286 (April 22) 1950.

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A recent clinical evaluation* of the effectiveness of certain drug combinations in acute upper respiratory infections, including the "common cold," clearly demonstrated A-P-Cillin to be, by far, the superior preparation.

It was found that 97.5% of the patients receiving A-P-Cillin were completely asymptomatic or improved at the end of the 72 hour treatment period.

Other commonly used preparations brought only 54% and 47% relief by the end of the same period.

To relieve distressing nasopharyngeal and constitutional symptoms, and to prevent secondary upper respiratory complications, prescribe—

White's A-P-CILLIN

Each tablet contains:

Procaine Penicillin G		100,000 units
APC	Acetylsalicylic acid	2½ gr.
	Phenacetin	2 gr.
	Caffeine	½ gr.
Phenyltoloxamine Dihydrogen Citrate (antihistamine)		25 mg.

The usual adult dose of A-P-Cillin is 2 tablets administered three times per day. Clinical experience indicates that treatment should be continued for not less than seventy-two hours. For optimal effect, the tablets should be taken at least one hour before or two or more hours after meals.

White Laboratories, Inc., Kenilworth, N. J.

*McLane, R. A.: Clinical Evaluation of Combined Drug Therapy in Acute Upper Respiratory Infections, J. M. Soc. N. J. 49:509 (Dec.) 1952.

nal Mortality Case Study Committees of the Michigan State Medical Society and the Wayne County (Detroit) Medical Society.

In view of the danger attendant upon this favorite maneuver of the "showmanship" days of a past era in obstetrics, it is fit and proper that it no longer has any niche of essentiality in the modern obstetrician's armamentarium of procedures. The procedure should be used only on a second twin when necessary and in the special situation in transverse presentation described above.

CHARLES S. STEVENSON, M.D.
Detroit

►TO THE EDITORS: Cesarean section, to some extent, has replaced the need for version and extraction. However, there are three instances in which the procedure can and should be used:

1] The procedure may be employed in case of a prolapsed cord, with complete dilatation, when forceps delivery would be too dangerous, difficult, or prolonged.

2] The method is of value in some cases of transverse presentation with complete dilatation in which disproportion is not evident and vaginal delivery seems entirely likely. This is especially so if the fetus is dead or the cord prolapsed.

Transverse presentations can usually be converted to cephalic or breech presentations during the last two months of pregnancy.

3] In a very occasional case, the patient enters the hospital fully dilated and with severe hemorrhage. The delivery room is immediately available whereas it would take thirty or forty minutes to ready the operating room for a cesarean section. Can the patient survive loss of blood that long or is immediate delivery by version and extraction the thing to do? I have done the procedure three times in the past with the loss of 1 baby and survival of all of the mothers.

These deliveries were all done in the days before blood banks made blood readily available. Today one might be inclined to give the patient a transfusion and then do a cesarean. One has to judge whether the amount of bleeding is too much and too rapid to warrant the delay in cross matching and cesarean. Possibly, in such cases, version and extraction is a lifesaving procedure.

PHILIP H. ARNOT, M.D.
San Francisco

►TO THE EDITORS: Internal podalic version and extraction is advisable only under the two following circumstances:

1] In certain cases of prolapse of the cord with the cervix fully dilated

2] In order to deliver the second twin when not already presented by the breech

This operation has been performed only for these indications for approximately eight years at the Sloane Hospital for Women. Previous to that, version and breech extraction constituted the largest single cause of birth injury, in spite of the fact that it was not often done at the Sloane Hospital.

CHARLES M. STEER, M.D.
New York City

► TO THE EDITORS: I read with interest the article on internal podalic version by Drs. Keettel and Crealock. I heartily agree that internal podalic version with extraction should be a very rare procedure and that its only indication is the transverse presentation of a second twin. This method should be shelved along with other obsolete procedures that are still mentioned in our modern textbooks.

I do not feel that prolapse of the cord in a vertex presentation with the cervix completely dilated is an indication for internal podalic version when the presenting part is above the level of the spines. Whenever the head remains above this level, with dilation of the cervix complete, other complications just as serious as the prolapsed cord are present which are sufficient indications for a cesarean section.

EUGENE S. AUER, M.D.

Denver

► TO THE EDITORS: Internal podalic version and extraction is indicated in selected cases of dystocia resulting from abnormalities of presentation, attitude, and position; in specific instances of prolapsed cord; when the second twin presents in the transverse; and in rare instances of failed forceps. It must be a planned procedure and not a measure of desperation or of last resort.

In specific cases of transverse presentation, face, brow, unengaged occipitoposterior position, or failed forceps, internal podalic version and extraction is indicated if, of the procedures available, this method alone offers the least hazard for the mother while not unduly jeopardizing the infant.

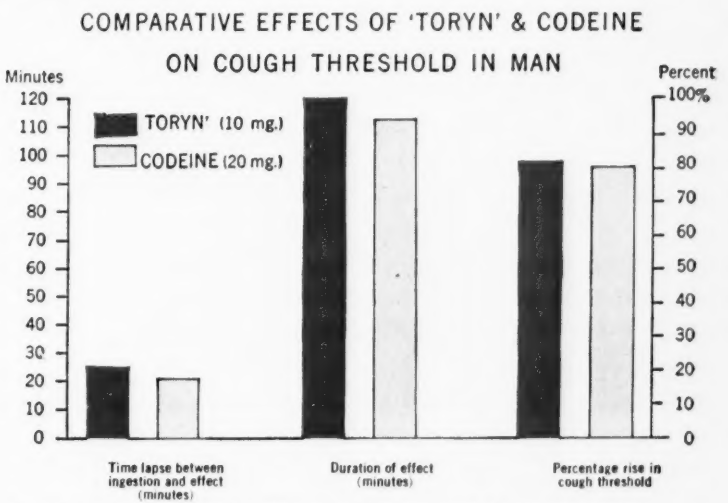
In determining the operative procedure of choice in these obstetric complications, it is well to recall that cesarean section is associated with a low but significant maternal mortality, that it does not necessarily guarantee a surviving infant, and that the individual who has had a cesarean section and who continues her reproductive career is handicapped because of this previous section. Also, in determining the procedure of choice, internal podalic version and extraction must not be considered in any obstetric complication except under the following circumstances:

1] Complete cervical dilatation or a completely dilatable cervix with a well-formed lower uterine segment
2] No cephalopelvic disproportion, either absolute or relative
3] Intact or but recently ruptured membranes
4] The lower uterine segment not abnormally thin
5] An unengaged or easily disengaged presenting part
6] The uterine tone not abnormally increased and the uterus relaxed completely under surgical anesthesia obtained with ether
7] No contraindications for ether anesthesia
8] A living and undamaged baby, weighing less than 4,200 gm.
9] An experienced operator
10] Adequate facilities

In the absence of any one or a combination of these conditions or if there is a doubt concerning the presence of any one of these conditions, version and extraction is definitely and emphatically contraindicated.

Human study shows 10 mg. of 'Toryn' equal in antitussive effect to 20 mg. of codeine

Dr. Magnus Blix[1], collaborating with Prof. Ernst Bárány, at the University of Upsala, Sweden, compared the effects of 'Toryn' and codeine on the human cough threshold. Using a new technique involving ammonia gas inhalation, they found that 10 mg. of 'Toryn' produced an antitussive effect† equal to that of 20 mg. of codeine. Results of this controlled study on 30 volunteers are presented in the graph below.



1. Blix, M.: On the Antitussive Effect of (β-diethylaminoethyl 1-phenylcyclopentane-1-carboxylate) ethanedisulfonate, S.K.F. ('Toryn'). *In manuscript.*
†(Average percentage rise in cough threshold) x (duration of activity)

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★T. M. Reg. U. S. Pat. Off. for caramiphen ethanedisulfonate, S.K.F.

I agree with Drs. Keettel and Crealock that internal podalic version and extraction is infrequently indicated; that it is contraindicated in the management of cephalopelvic disproportion; and that it should not be employed in the management of placenta previa. Likewise, I agree with them that statistics show that this is a hazardous procedure for both baby and mother. However, I believe that in rare instances of dystocia due to abnormalities of presentation, attitude, and position, it is the procedure of choice. Therefore, I believe that its use should not be restricted entirely to instances of prolapsed cord with unengaged head or to those cases in which the second twin presents in the transverse.

CHARLES P. MC CARTNEY, M.D.
Chicago

► TO THE EDITORS: In the past, many different obstetric predicaments were accepted as indications for delivery by version and extraction. These situations, more often than not, were complex ones in which the maneuver was difficult to accomplish. Despite the difficulties and obvious hazards, versions were attempted. The operator reconciled himself with the belief that this procedure was the only solution of the problem. Versions, even when done under favorable circumstances by experienced obstetricians, have inflicted all degrees of trauma on both mother and child.

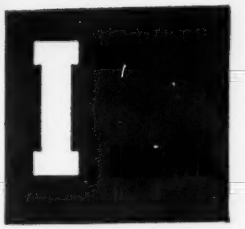
The present day obstetrician who conscientiously applies the modern methods of diagnosis and treatment will encounter the need for version and extraction only on rare occasions. Rigid indications for this operation, as for any other, cannot and should not be established because the occasional life may be sacrificed. However, the performance of a version, regardless of indication and outcome, should immediately initiate a thorough and critical evaluation of the patient, her pregnancy, and labor. Frequently this analysis will reveal that evidence of a potential or impending dystocia was present at a time when the ultimate problem could have been avoided by appropriate management. In the light of modern knowledge there is rare justification for any procedure that results in trauma greater than that of low cervical cesarean section.

During the past six years at the Pittsburgh Hospital the incidence of internal podalic version with breech extraction has steadily declined from 2 to 0.8%. This fact, together with a decrease in potentially difficult midforceps deliveries, has increased the cesarean section rate but decreased the fetal morbidity and mortality.

WILLIAM E. GIBSON, M.D.
Pittsburgh

► TO THE EDITORS: I have very little to add or subtract to the article by Drs. Keettel and Crealock. Their argument is sound and their statistics are generally good.

Version and extraction has undergone many changes in popularity. Known to the ancients, it was not included in the encyclopedic



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Crampton, C. W., The Merck Report, 57:26 (1948)
Kimble, S. T., and Steiglitz, E. J., Geriatric 7:20 (1952)

compilations of Paulus Aegineta which fell into the hands of the Arabs after the fall of the Roman Empire. The operation was lost for a thousand years and was not revived until Roesslin, having access to another encyclopedic compilation done by Soranus, mentioned it in the first printed obstetrics, *Rosengarten*.

It was not, however, performed for nearly another half century, when the French surgeon, Paré, actually did it. The operation was thus revived, received considerable attention, and was very useful, but fell again into desuetude with the general introduction of the obstetric forceps about 1730 to 1750.

In the early part of this century, the procedure was revived by Irving Potter of Buffalo. Potter became expert at the operation but was never able to reduce his mortality rate below that of normal expectancy for an average obstetric practice. In his favor, it may be said that he probably was the most dexterous operator and exponent of the operation that the world has known. Today, with modern cesarean section, there is little need to subject infant and mother to the risk of version and extraction.

I hardly believe that version on the second twin would ever be called an operation of election. In some instances it would certainly be an operation of necessity and, as Drs. Keettel and Crealock have pointed out, it can then be done with a relatively low rate of mortality.

WILLIAM F. MENGERT, M.D.
Dallas

Symptoms of Common Duct Stones*

QUESTION: When should the common duct be explored?

Comment invited from
H. Vern Sharp, M.D.
Albert L. Evans, M.D.
Ralph V. Byrne, M.D.

►TO THE EDITORS: The suggestion of Drs. E. Lee Strohl, Willis G. Diffenbaugh, and Vernon Guynn to use nausea and vomiting in biliary disease as a criterion to explore the common duct offers a new thought. Evaluation of my own cases of surgical gallbladder disease shows that the incidence of nausea and vomiting is greater than the presence of common duct stones.

The common duct should be explored when any of the following precepts pertain:

1] History of jaundice is given
2] Small stones are present in the gallbladder and the cystic duct is patent
3] The common duct is dilated and yellowish-white or the duct is thickened, indicating cholangitis
4] At palpation of the common duct there is any question of stones being present
5] Pancreatitis is demonstrable
6] Sediment is aspirated from the common duct.

Because of the high incidence of stones in the common duct when stones are present in the gallbladder and because there is no group of symptoms or physical findings either before or at the time of operation which can serve justly to exclude the presence of stones in

*MODERN MEDICINE, Nov. 15, 1952, p. 89.

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the gallbladder, I have explored the common ducts more often than I have found stones.

H. VERN SHARP, M.D.
Akron

► TO THE EDITORS: The question of when to explore the common duct presents itself constantly to the gallbladder surgeon. Because stones occur in the bile ducts, in 15 to 20% of cases of cholelithiasis, it is apparent that the meticulous surgeon will explore many common ducts.

Although an exploration of the ducts by the experienced surgeon adds little to the morbidity, I do not believe that the common duct should be explored routinely with cholelithiasis. The most common indications for exploration are palpation of a stone in the duct; jaundice at the time of operation or associated with previous attacks; recurring attacks of biliary colic with or without chills and fever; dilated or thickened common duct with questionable palpation of a stone; multiple small stones in the gallbladder or in the cystic duct; and dark bile with sediment aspirated from the common duct.

Any duct suspected of containing a stone should be explored. There will undoubtedly be some ducts opened and explored in which no stone can be found but unless these ductal stones are looked for, many will be left, thus necessitating further surgery for the unfortunate individual.

ALBERT L. EVANS, M.D.
Atlanta

► TO THE EDITORS: The decision to explore the common duct rests on the experience of the operating surgeon and the conditions that are found at the operating table. The presence of disease in the gallbladder alone is not sufficient to warrant common duct exploration.

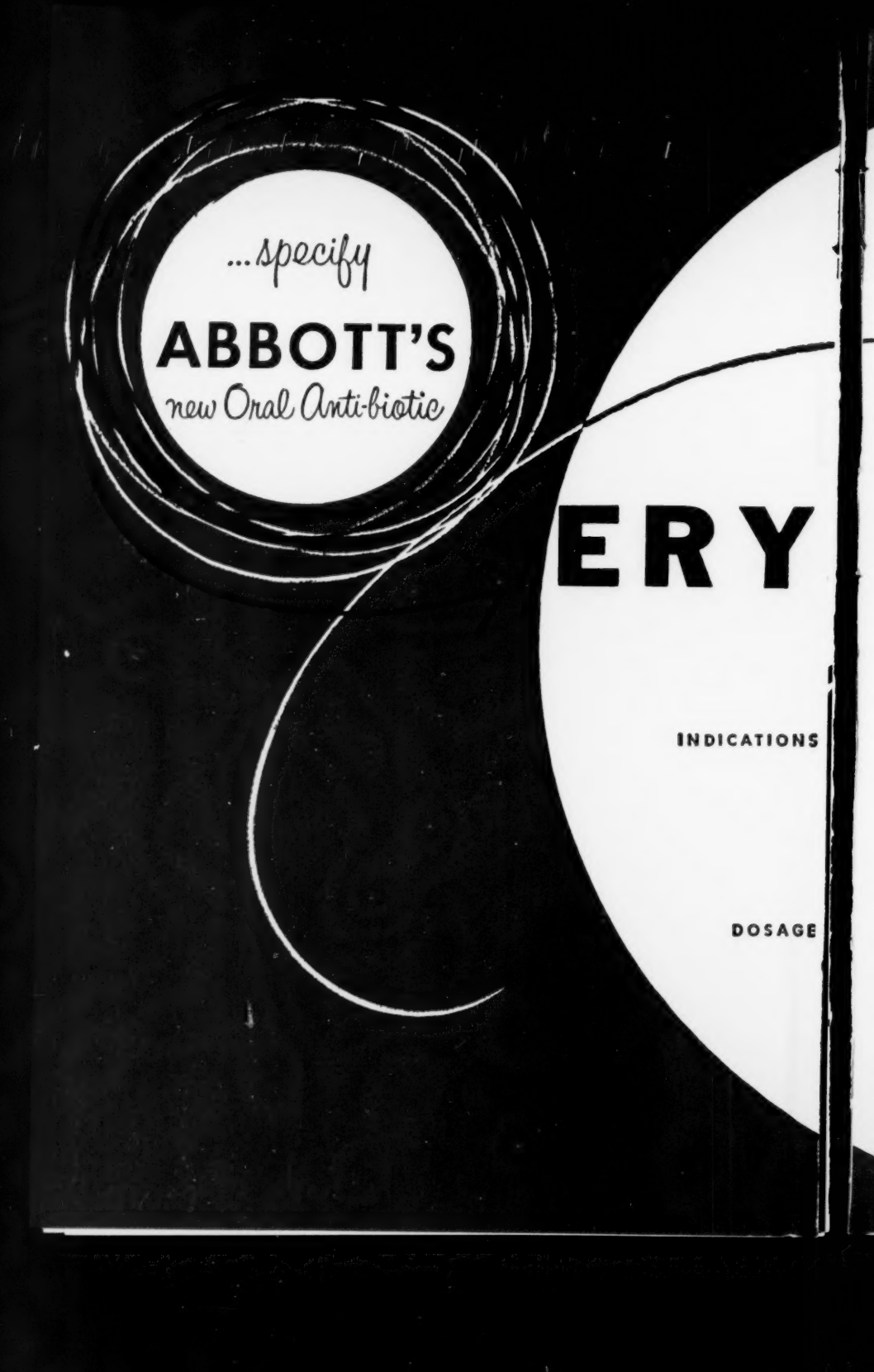
Occasionally, a patient with a history of jaundice is operated upon and the common duct exploration fails to reveal a stone. These instances very clearly demonstrate that none of the indications for common duct exploration, when considered singly, is foolproof.

The decision to explore the common duct should be made on the basis of the appearance of the gallbladder and the common duct and the impressions gained by visualization and palpation at the operating table. The indications that have withstood the test of time are:

- History of jaundice
- Palpation of stones in the common duct
- Dilatation or thickening of the common duct
- Small stones in the gallbladder with a patent cystic duct
- Abnormal bile aspirated from the common duct
- Thickening of the head of the pancreas
- Stones in the gallbladder in patients past 60 years.

In doubtful cases the above-mentioned indications will be of invaluable aid. Nausea and vomiting are symptoms so commonly associated with upper abdominal pathology that I would hesitate to list them as indications for common duct exploration.

RALPH V. BYRNE, M.D.
Los Angeles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INDICATIONS
DOSAGE

E *specially effective against gram-positive organisms resistant to other antibiotics.*

L *ow toxicity; gastrointestinal disturbances rare; no serious side effects reported.*

S *pecial "high-blood-level" coating.*

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(Erythromycin, Abbott)

Pharyngitis, tonsillitis, scarlet fever, erysipelas, pneumococcic pneumonia, osteomyelitis, pyoderma. *Also other organisms* susceptible to its action, which include staphylococci, streptococci, pneumococci, *H. influenzae*, *H. pertussis*, and corynebacteria.

Total daily dose of 0.8 to 2 Gm., depending on severity of the infection. A total daily dose of 0.4 Gm. is often adequate in the treatment of pneumococcic pneumonia.

For the average adult an initial dose of 0.1 to 0.4 Gm. is followed by doses in the same range every four to six hours.

For severely ill patients doses up to 0.5 Gm. may be repeated at six-hour intervals if necessary. Satisfactory clinical response should appear in 24 to 48 hours if the causative organism is susceptible to ERYTHROCIN. Continue for 48 hours after temperature returns to normal.

Abbott

1. McGuire et al. (1952), J. Antibiotics & Chemo., 2:281, June. 2. Heilman et al. (1952), Proc. Staff Meet. Mayo Clin., 27:385, July 16. 3. Haight and Finland (1952), New Eng. J. Med., 247:227, Aug. 14.

D iagnostix

Here are diagnostic challenges presented as they confront the consultant from the first clue to the pathologic report. Diagnosis from the Clue requires unusual acumen and luck; from Part II, perspicacity; from Part III, discernment.

Case MM-235

THE CLUE

ATTENDING M.D: I would like you to see a 2-day-old baby with increasing abdominal distention and bilious vomiting. The bowels have not moved since birth. Right this way, please. *(They enter nursery.)*

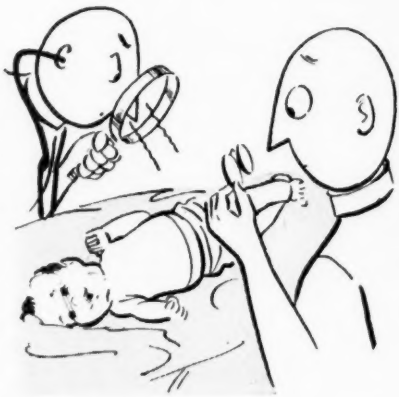
VISITING M.D: *(Uncovers baby)* Well, see what we have. Before I have a chance to examine the anus, normal meconium is passed: That eliminates the possibility of intestinal obstruction of the newborn, organic atresia, and malrotation of the bowel. *(Examines baby)* Nothing noteworthy by physical examination. Were the delivery and prenatal period normal?

ATTENDING M.D: Yes. Birth weight was 8 lb., the distention was progressive from birth. Perhaps we were too hasty in calling for consultation. Time seems to have solved the problem.

VISITING M.D: I am not so sure. Let's watch the child's progress for a few days.

PART II

ATTENDING M.D: *(Three days later)* The vomiting and abdominal distention ceased after the meconium was passed. The baby had a normal bowel movement later that day and she appears to be well.

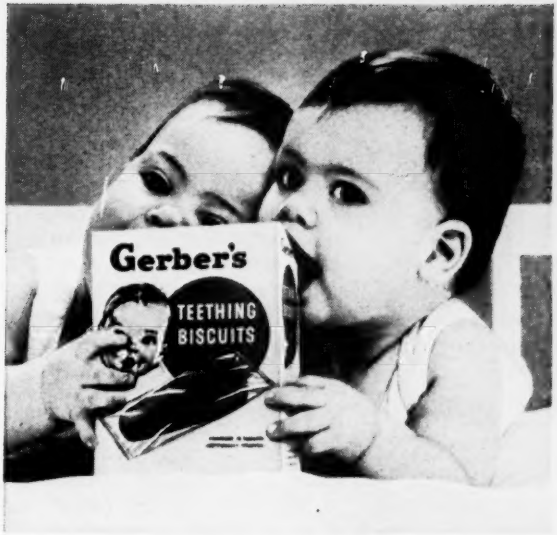


VISITING M.D: We may have heard the last of the trouble, but I doubt it.

ATTENDING M.D: *(On next day's rounds)* You were correct about that baby with the distention. She has had a relapse.

VISITING M.D: *(Looking over chart)* Vomiting was the first symptom within twelve hours after first feeding; the vomiting became more frequent, with attendant bowel distention and delay in passage of meconium; then a typical amelioration of symptoms.

New way to help teething babies →



Gerber's Teething Biscuits... the first ever made specially for teething babies!

Safer → Firmer texture gives less opportunity for aspiration of crumbs. (Less messy for young mothers, too!)

gentler → Smooth hard surface of Gerber's Teething Biscuits gives plenty of chance for chewing and biting exercise . . . yet is easy on tender gums.

Wholesome → Teething Biscuits contain added whole milk solids, dried yeast, dicalcium phosphate. Light, mild flavor . . . lasting firmness so baby doesn't digest a quantity that might spoil appetite.

Easy to hold → Shaped for easy grasping by small hands . . . to help give practice in hand-to-mouth coordination.

Sanitary → Individually wrapped for clean handling of single biscuits—when "airing" or traveling with baby.

Babies are our business...
our only business!

Gerber's BABY FOODS

4 CEREALS • 40 STRAINED & JUNIOR FOODS
10 MEATS

The cause of the obstruction is low in the large bowel.

ATTENDING M.D: I mentioned this case to the surgical consultant in the hall when the symptoms recurred. He thought we should consider surgical intervention after roentgenograms were made.

VISITING M.D: I see that you ordered a barium enema this morning. Let's see the pictures. *(They go to the Radiology Department.)*

PART III

RADIOLOGIST: The colon is dilated, with narrowing at the rectosigmoid junction. I note greatly distended loops of gut with infrequent peristalsis. After the barium enema, normal feces were passed and the infant seemed better.

VISITING M.D: What sort of narrowing is there?

RADIOLOGIST: *(Pointing to film)* A string-like narrowing at the rectosigmoid and above that the entire colon is dilated. It is hard to get a clear discrimination between the large and the small intestine. I remember a similar case last year in which only after 3 roentgen examinations were we able to demonstrate the string-like constriction. Apparently it is inconstant but can be demonstrated if one persists. I think the picture is quite characteristic. Are there any clues in the laboratory and physical examinations?

ATTENDING M.D: No.

VISITING M.D: This disease of young babies is not as uncommon as is usually thought. In the less severe cases the symptoms are not recognized until childhood after a long latent period following a neonatal incident. Of the few patients surviving infancy, none is symptom free. Mortality is high, especially when the diagnosis is incomplete. The length of the affected bowel and the severity of the consequent disease vary greatly.

PART IV

ATTENDING M.D: I spoke to a psychiatric consultant about this disorder yesterday and . . .

VISITING M.D: I see you've been busy collecting opinions in the hall.

ATTENDING M.D: *(Unperturbed)* He said that often Hirschsprung's disease is psychologic in origin and the genesis is in bowel neglect of conflicts. He has had some success with psychotherapy of a child of 10.

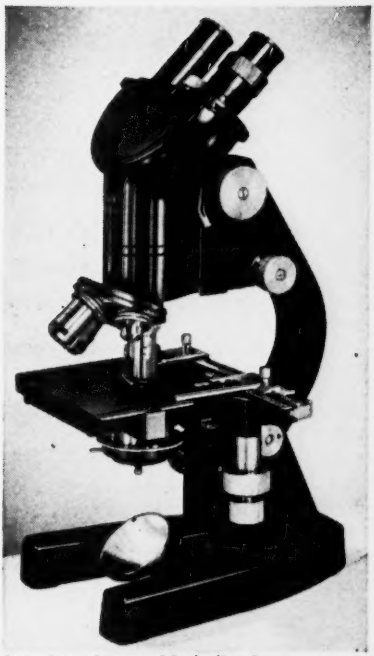
VISITING M.D: It is quite possible to have success with psychotherapy with organic disease, you know. The symptoms are functional. What was his evidence for psychic genesis?

ATTENDING M.D: I guess the megacolon and constipation in his malnourished child improved. What is the organic basis of the disease?

VISITING M.D: It seems to me to be irrefutable—Hirschsprung's disease is one thing, dyschezia with colonic enlargement because of an unresponsive and distended rectum is another. With Hirsch-

(Continued on page 202)

for **Lifetime**
accuracy and precision



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*Beckman, H.: Pharmacology in Clinical Practice, Philadelphia, W. B. Saunders Company, 1952, p. 361.

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sprung's disease the colon is both widely dilated and hypertrophied with a funnel-shaped narrowing of the lower sigmoid and rectum. Failure to recognize this by radiologic examination has obscured the true picture of the disease and led to conflicting reports about prognosis and forms of therapy. Neonatal colonic dilatation can always be demonstrated if sought, and there should be a preparatory washing out of both the rectum and the colon.

ATTENDING M.D: You describe its appearance well enough, but what about the etiology of such a condition? What is the organic nature of this disorder?

VISITING M.D: We don't have an organic cause demonstrated. But neither do we know the etiology of diabetes. Because of two things I believe the psychologic etiology is untenable: *One,* I have studied 7 infants, observed from birth, with the symptoms in the first twenty-four to seventy-two hours. There have been larger series of infants with onset up to 2 months of age. The lesion starts too soon. Several die with the exacerbations. *Two,* after one month, the muscle of the colon is hypertrophied. The autopsies of children dead at the age of 3 days or 3 months invariably reveal absence of the myenteric ganglion cells in the rectum. Below the dilatation these cells are absent. How do they disappear, or why are they absent? Therein lies the answer we must seek.

ATTENDING M.D: What about surgery?

VISITING M.D: Surgery has little place at the time of the earliest symptoms, no matter how serious they seem. A longer observation is needed to determine the severity of the case. In some patients who deteriorate in the following months or weeks, the affected segment is too long for resection and approximation of the upper segment to the anus.

ATTENDING M.D: I'm not entirely clear in my mind concerning this dyschezia.

VISITING M.D: Not surprising . . . no one else is. With dyschezia the average child responds well to training, enemas, and purgatives provided a careful watch is kept for the overloaded rectum which heralds an arrest in the return to normal.

ATTENDING M.D: Does the syndrome of constipation, distention, and vomiting in the neonatal period relieved by the passage of meconium, with or without local intervention, always mean a diagnosis of Hirschsprung's disease?

VISITING M.D: No. However, while a clear account of a neonatal episode is of inestimable value in establishing the diagnosis, it is sometimes not available. The autopsy findings establish the identification of the malady. I believe it is present from birth; at least that is what I mean by the diagnosis. I wish we had more reported observations on these early dysfunctions seen in our hospital nurseries.

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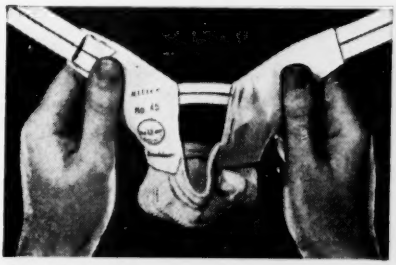

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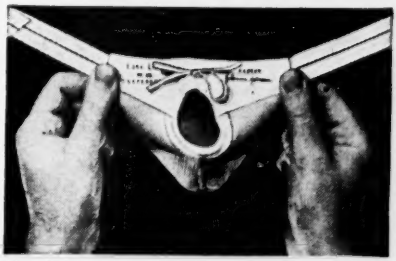
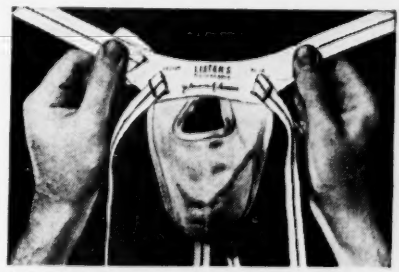


No. 101 Without legstraps. Drawstring in yoke can be adjusted. Knitted pouch is suspended from sides, for upward lift. L.M.S.....$1.00



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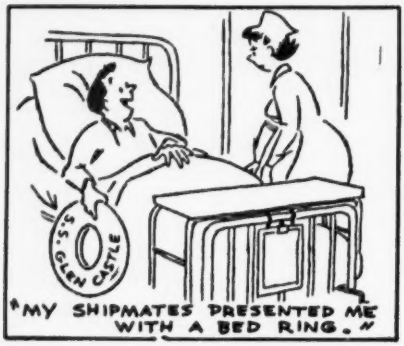
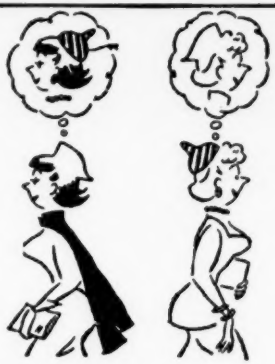
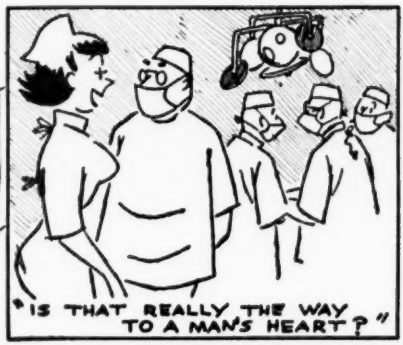


"MY SHIPMATES PRESENTED ME WITH A BED RING."



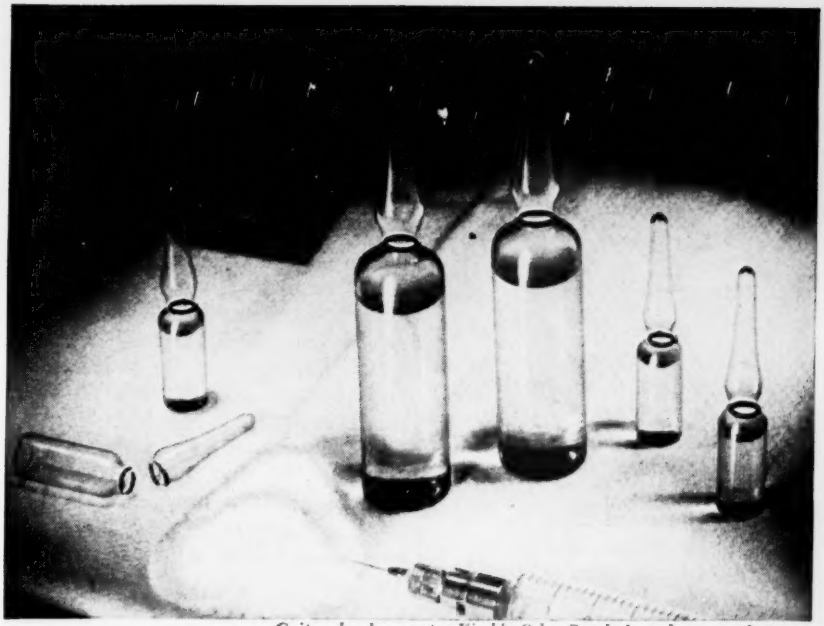
"IF THE DOCTOR EVER ORDERS US TO REDUCE, WE'LL HAVE TO SELL OUR TV SET."



"IS THAT REALLY THE WAY TO A MAN'S HEART?"

"HE HASN'T COME OUT OF IT YET. HE'S STILL TRYING TO BLOW THE FOAM OFF HIS MEDICINE."

"THIS IS A NICE PLACE TO VISIT, BUT I WOULDN'T WANT TO LIVE HERE."



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BASIC SCIENCE *Briefs*

Endocrinology

Temperature Effect on Cortisone

The toxicity of cortisone acetate is increased for mice by environmental temperatures of 35 to 37° C. Males especially are affected. Dr. George H. Scherr of Creighton University, Omaha, finds that the deleterious effects of cold, —5 to 7° C., are eliminated when the animals are injected intramuscularly with 0.5 mg. of the drug every forty-eight hours during the eight days of exposure; treated animals survive but the untreated ones die. These data indicate the necessity for use of uninfected, treated control groups in each experiment with the hormone.

Science 116:685, 1952.

Oncology

Accessory Limbs in Newts

Some carcinogens are capable of inducing not only neoplasms, but highly organized growth as well. Coal tar, some coal tar fractions, beryllium hydroxide, and petroleum jelly will stimulate neogenesis when injected into newts, resulting in the growth of a well-formed extra limb. Dr. Charles Breedis of the University of Pennsylvania, Philadelphia, reports that the injection area shows stages of necrosis, degeneration, dedifferentiation, and finally blastema formation, which eventually gives rise to the muscle and bone of the new appendage. Agents such as benzpyrene, acetylaminoflourine, and scarlet red, which cause equal tissue damage, have no effect on limb induction. Results support the hypothesis that the effective agents directly stimulate the blastema-forming tissue of amphibians.

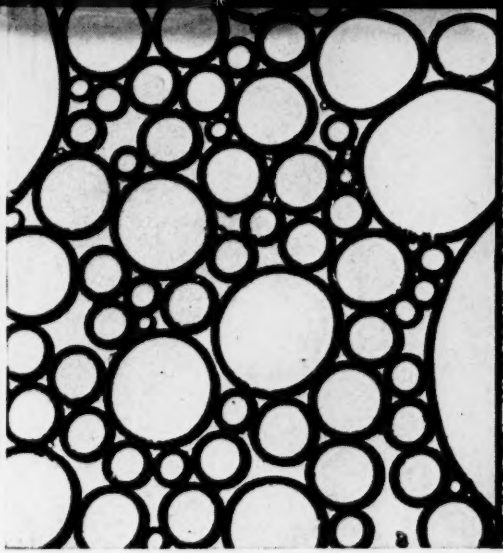
Cancer Research 12:861-866, 1952.

Physiology

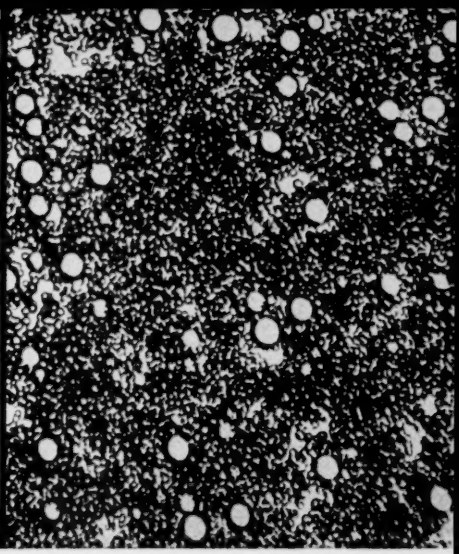
Arterial Spasm and Pulse Reduction

Vasomotor nerves in dogs can produce sufficient spasm of the muscular arteries to reduce by 75% the peripheral pulses and by 50% the blood pressure distal to the contraction. While direct stimulation of the sciatic nerve produced these effects in anesthetized animals, Drs. Robert S. Alexander and Adrian Kantrowitz of Western Reserve University, Cleveland, find that the constriction caused by trauma to the arterial walls does not elicit an acute response of the femoral system great enough to alter the transmitted pulse pressures or account for the ischemia. Clinically, diseased vessels and edematous tissues may be complicating factors affecting the degree of localized blood deficiency.

Surgery 33:42-47, 1953.



1 *Oil dispersion (x133). Large irregular globules fail to mix readily with fecal mass. Phenolphthalein is not evenly distributed to stimulate peristalsis. Action may be sporadic and evacuation incomplete.*



2 *The fine oil emulsion (x133) of Agoral. The small, uniform globules and the phenolphthalein mix readily with the bowel content, producing peristalsis by more uniform lubrication and stimulation.*

Which Laxative is Better—

COARSE DISPERSION OR FINE EMULSION?

Coarse dispersions are unstable, and erratic in their effects. Any physician can recognize the superiority of the fine Agoral emulsion (*at right, above*) compared with an ordinary oil-in-water dispersion (*left*).

Free-floating oil is distasteful and often regurgitated. Large oil globules tend to coalesce and form pools in the gut, which may seep past the sphincter as anal leakage.

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The fine emulsion of Agoral is palatable and will not distress a sensitive stomach. It assures more uniform dosage and distribution of the active ingredients, more uniform clinical results.

Its thorough admixture with the bowel content gives effective, uniform lubrication of the fecal mass as well as the canal. There is no loose oil to cause anal leakage.

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Agoral is emulsified exclusively with refined white mineral oil, purified white phenolphthalein, agar-gel, tragacanth, acacia, egg-albumen and glycerin, by a special process similar to that used for homogenizing milk.

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A marked advance in oral estrogenic therapy, SULESTREX is a pure, stable, water-soluble, crystalline compound, deriving its estrogenic activity entirely from estrone. It is *not* a mixture of estrogens, nor does it contain any inactive steroids or uriniferous ingredients.

Reich and associates[1], in a recent continuing study, observed that SULESTREX " . . . *is a clinically effective oral estrogenic substance, easy to administer and extremely well tolerated . . . with an amazingly low incidence of side reactions.*"

Prescribe it with the assurance that you are using as effective estrogen therapy as science has yet created. Abbott

1. Reich, W. J., et al. (1952): A Recent Advance in Estrogen Therapy. II. American J. Obst. & Gynec., 64:174, July

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medicine BROAD

GERMANY

Therapeutic Epidural Anesthesia. Epidural segmental anesthesia is a fairly simple procedure applicable to many conditions. Excellent therapeutic results are claimed for lesions as varied as neuralgia, infectious hepatitis, intestinal motility disturbances, traumatic shock, and vasomotor anomalies of the lower extremities. Dr. Martin Bergmeyer of Krankenhauses St. Georg, Hamburg, first injects the epidural space with up to 100 cc. of saline to establish the passage of the subsequent anesthetic injection, 30 to 45 mg. of Pantocain in up to 10 cc. of Kollidon, to all the nervi communicantes, the sympathetic chain, and the splanchnic nerves. Epidural anesthesia is technically simpler and more successful than paravertebral block of the sympathetic chain.

AUSTRIA

Treatment for Noncardiac Swelling of the Ankles. Injections of heparin or hyaluronidase are effective therapy for swelling of the ankles caused by local conditions, such as periarthritis, posttraumatic or postphlebitic edema, or allergic reactions. The injections are made along the margin of the swelling and are followed by gentle massage. In the experience of Dr. W. Breu of Vienna, heparin is more useful in cases with abundant thin fluid collection, mainly of an inflammatory type, while hyaluronidase is preferable for the swellings that are caused by chronic fibrotic processes.

SWITZERLAND

Treatment of Pulmonary Embolism with Ganglion Blocking Agents. Chief symptoms of pulmonary embolism are acute thoracic pain, superficial breathing, cold sweats, and feeling of imminent death, which may be caused by a reflex constriction of pulmonary and coronary vessels. To inhibit such a reflex, Drs. J.-P. Crosetti, C. A. Muller, and J. Pettavel of the City Hospital of Neuchâtel, Switzerland, suggest intravenous administration of a ganglion blocking agent, Pendiomid. The slow intravenous injection of 100 mg. of this agent at a rate of less than 20 mg. per minute freed 9 of 10 patients within thirty minutes of all subjective symptoms; the tenth patient was freed within an hour. Blood pressure did not drop below 30% of the initial level except in 1 case in

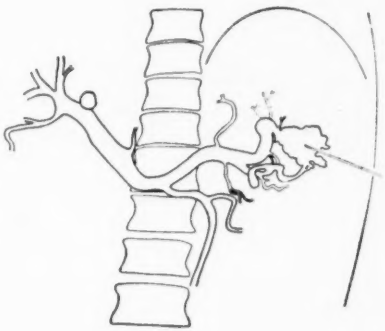
which the drug was given too rapidly. Respiratory excursions increased and the pulse rate remained unchanged. Such a therapeutic approach is considered more rational than the usual morphine medication and, by liberating respiratory movements, often obviates the necessity of administering oxygen. The injection can be administered as an emergency measure when facilities for oxygen therapy are not available.

FRANCE

Diagnostic Aid in Mediastinal Disease. Injection of air or oxygen into the mediastinum increases the contrast contours of the opaque organs, thus facilitating roentgenographic study, especially if planigrams are made. Drs. M. Bariéty, Ch. Coury, P. Choubrac, and P. Mathé of Paris give 14 examples of cases in which pneumomediastinum may aid the detection of cardiac and aortic aneurysms, bronchogenic cancer, thymoma, or cysts. The technic consists of injection of 300 to 600 cc. of air into the posterior mediastinum. The needle is introduced, using local anesthesia, through the trachea into the mediastinum. Pneumothorax or intravascular injection of air should be avoided. When properly performed, no ill effects result, the injected air being absorbed within ten days. The diagnostic value of pneumomediastinum increases if combined with angiocardiographic or angiopneumographic study, or both.

ITALY

Visualization of Portal System. Radiopaque material gives important diagnostic information of the portal system but has been practicable only when the patient is on the operating table with the abdomen



open and the portal vein directly visible. Drs. G. Sotgiu, C. Cacciari, and A. Frassineti of Bologna, Italy, now report a simple method by which the portal vessels can be studied after the percutaneous rapid injection of 20 cc. of radiopaque material into the spleen. Two to four seconds later the portal vessels may be well visualized, unless the splenic vein is obstructed. The procedure is useful in the investigation of disorders of any part of the portal system, including splenomegaly or diseases of the liver. A drawing of a radiogram made by this technic in a case of hypertrophic splenomegalic cirrhosis is shown in the illustration.

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Long-range Systemic Control

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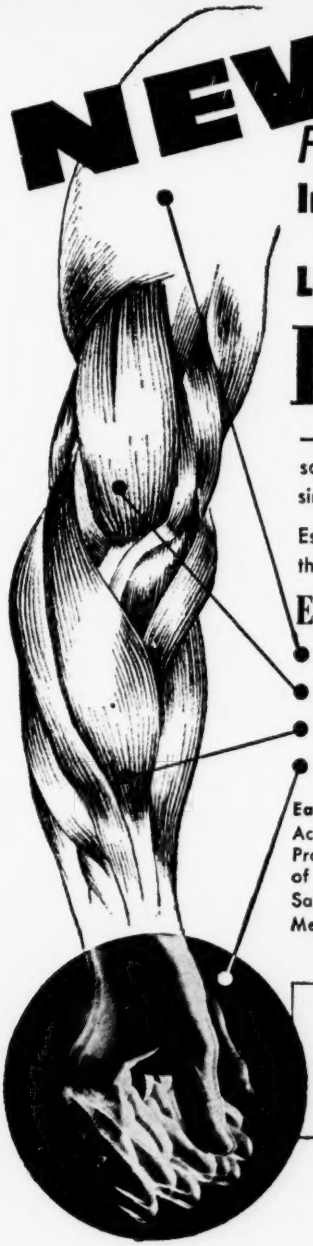
—features for the first time the reliable analgesia of salicylamide, the muscle-relaxing qualities of mephenesin, and the time-proved antiarthritic steroid, Ertron.

Especially valuable in the initial stages of arthritis therapy, when rapid relief from pain is indicated.



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- *alleviates pain in afflicted joints*
- *relaxes associated muscle spasm*
- *relieves skeletal muscle pain*
- *increases mobility of the joints*

Each Ertron-S-M capsule contains:
Activation products (activated vaporized ergosterol-Whittier Process—biologically standardized) having antirachitic activity of fifty thousand U.S.P. units..... 5 mg.
Salicylamide.....162 mg.
Mephenesin.....125 mg.

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LATE REPORTS *from Medical Centers*

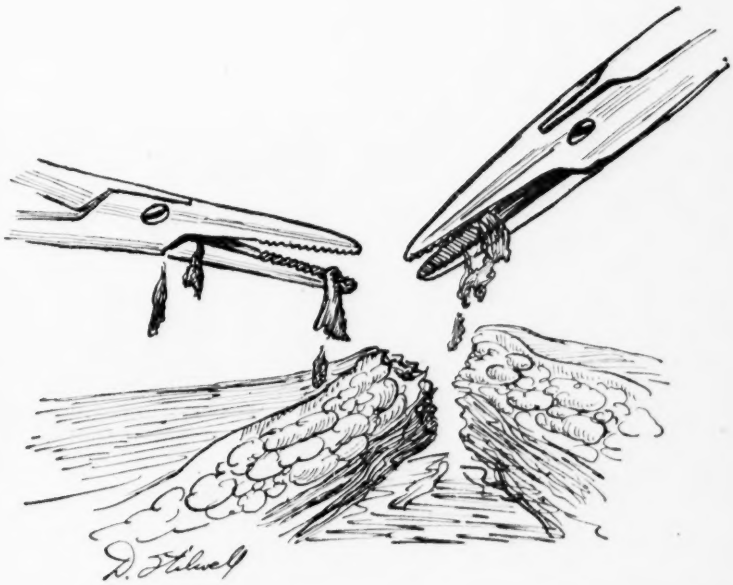
HARVARD UNIVERSITY, Boston--Cholesterol is manufactured in the body by isolated cellular elements rather than by the cell as a whole. Finely-minced liver tissue with no microscopically visible intact cells is more efficient in production of cholesterol than are suspended cells or entire slices of liver. Dr. Nancy L. R. Bucher observed synthesis of cholesterol in various tissue preparations after addition of acetate that contained radioactive carbon.

★ ROBERT B. BRIGHAM HOSPITAL, Boston--Motion may be restored to a painful, stiff, arthritic knee with the aid of a thin piece of nylon placed between joint surfaces. Using a sheet 0.003 to 0.005 in. thick, Dr. John G. Kuhns and associates staple the lining to bone with stainless steel on surfaces bearing no weight. Function was satisfactory about six months after operation in 58 of 70 knees.

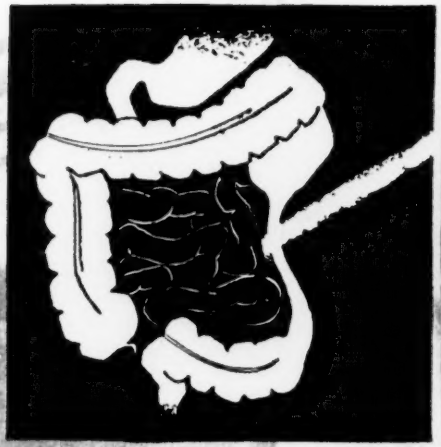
★ DUKE UNIVERSITY, Durham, N. C.--Cluster headache, so named by Dr. E. Charles Kunkle because the pain may occur in several brief episodes a day for weeks, resembles migraine but differs in rate, duration, lack of warning signals, and rarity of nausea and vomiting. Most patients are men. Attacks are often less than half an hour long. The nose is frequently congested on the same side as pain, and redness and watering of the eye occur. Headache is probably due to enlargement of sensitive cranial arteries.

★ UNIVERSITY OF MICHIGAN, Ann Arbor--Anti-clotting power 200 times that of dicumarol is possessed by Dipaxin (diphenylacetyl-1,3-indandione). Toxicity is correspondingly low. With oral doses of 30 to 50 mg., Dr. I. F. Duff and associates produce satisfactory prothrombin levels in twenty-four to forty-eight hours or less. Effects ordinarily last two to five days after the last dose but can be reversed in a few hours by intravenous injection of vitamin K_1.

★ VETERANS ADMINISTRATION HOSPITAL, New York City--So-called ingrown toenail is primarily a soft tissue infection produced by improper trimming of nails. For cure without deformity, Dr. David I. Schwartz employs standard medical procedures for infection, rather than surgery of nail or toe.



Efficient spasmolysis....



....in functional disorders

. . . such as irritable colon, emotional diarrhea, peptic ulcer, pyrosis; also for inflammatory diarrhea due to acute gastroenteritis or ulcerative colitis, and functional dysmenorrhea.

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...in an exceptionally pleasant-tasting elixir colored an appetizing orange-red. Supplied in bottles of one pint and one gallon. Samples on request.

1. Dripps, R.D., Selective Utilization of Barbiturates, J.A.M.A. 139:148 (Jan. 15) 1949.

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short REPORTS

Parasitology

Hepatomegaly with Amebiasis

Slight enlargement of the liver is noted in many cases of active amebic colitis although no actual parasitic invasion of the organ is demonstrable by histologic study. Autopsy records of 7 persons who died of *Endamoeba histolytica* infestations reveal greater than usual liver weights, report Drs. G. M. Carrera and E. H. Sadun of Tulane University, New Orleans. Guinea pigs infected with the parasite have more acute infection and greater degree of hepatomegaly than occur in human beings.

Am. J. Trop. Med. & Hyg. 1:962-964, 1952.

Experimental Medicine

Corneal Tuberculosis Treated with Isoniazid

Antituberculous chemotherapeutic agents may be assessed by study of reactions in induced tuberculous lesions of the cornea in mice and rabbits, since response parallels clinical experience in human beings. In mice, isoniazid used alone suppresses the infection only during treatment and effects are not enhanced by the addition of para-aminosalicylic acid. However, when isoniazid and streptomycin are given together, control of the disease is greatly increased. In rabbits, the hydrazine derivative alone is more active than streptomycin alone, probably evincing bactericidal as well as bacteriostatic properties. Although the mouse usually exhibits more natural resistance to corneal tuberculosis, Drs. Roy Goulding and J. M. Robson of Guy's Hospital, London, believe that the species difference in this instance may result from the greater effectiveness of the compound at the higher body temperature of the larger animal. This potentiated activity of isoniazid has been observed in pyrexial patients.

Lancet 263:849-853, 1952.

Gastroenterology

Bile Duct Anastomosis

Stricture is more frequent with than without use of latex rubber T tubes in dogs after biliary anastomosis. Also, bacterial infection is more common with a T tube. However, say Drs. Banning G. Lary of the University of Illinois, Chicago, and John R. Scheibe of the Gilfillan Clinic, Bloomfield, Ia., drainage is advisable in all common duct anastomoses since bile peritonitis is far more frequent in the animals in which no external drainage is used after transection and anastomosis of the duct. Fibrosis and leukocytic reaction in the duct wall increase when a T tube remains in place for two months.

Surgery 32:789-795, 1952.

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NOVALENE, with its many *active* ingredients provides not only rapid relief with prolonged effect, but is also remarkable for its valuable prophylactic action.

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Formulae:

NOVALENE	Phenobarbital (Warning—May be habit-forming)	¼ gr.
	Ephedrine Sulfate	⅛ gr.
	Potassium Iodide	2½ gr.
	Calcium Lactate	2½ gr.
HISTA-NOVALENE	Sodium Phenobarbital (Warning—May be habit-forming)	¼ gr.
	Ephedrine Sulfate	⅛ gr.
	Potassium Iodide	2½ gr.
	Calcium Lactate	2½ gr.
	Pyrilamine Maleate	20 mg.

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Arthritis

Glycine Metabolism

The fasting level of serum glycine declines more than 15% in most cases of active rheumatoid arthritis after intravenous administration of sodium benzoate. The decline persists for at least an hour. Similar changes occur in patients with active rheumatic fever or disseminated lupus erythematosus. Serum glycine remains constant in healthy persons or patients with hypertrophic osteoarthritis. Dr. H. M. Lemon and associates of Boston University and the Veterans Administration, Boston, believe that the reaction to the benzoate test suggests metabolic abnormality affecting connective tissues. Evaluation of the response may assist in earlier recognition of rheumatoid arthritis and in objective evaluation of arthritic symptoms.

J. Clin. Investigation 31:993-999, 1952.

Orthopedics

Cancellous Bone Chips

New bone that forms about cancellous chips transplanted into muscle arises solely from the covering cells of the chips or from associated marrow cells. This fact has a practical meaning for the surgeon attempting to set up osteogenic centers in bone defects. First, since the new bone is derived from the surface of the chips, autografts are preferable to homografts. Homograft cells either would fail to multiply or would act as an antigen and be destroyed. Second, chips should be taken from cancellous regions or from young growing shaft, since both these types of graft have many more osteogenic cells on the surface than does compact adult bone. Third, material taken for transplant should be handled gently, kept moist, and introduced near capillaries in living tissue. However, even dead bits may act as a support for new osteoblasts originating in the host. The claim is sometimes made that connective tissue can be stimulated to produce bone cells as the result of metaplasia induced by chemical substances inherent in the chips. Evidence against this idea was obtained by Arthur Ham, M.B., and Stuart Gordon, M.B., of the University of Toronto. Untreated autogenous chips of cancellous bone and chips previously frozen and thawed three times were inserted into muscles of 5 dogs. New osseous tissue appeared in all the animals, but only around the untreated implants.

Brit. J. Plast. Surg. 5:154-160, 1952.

"He keeps asking for your wife."

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Metabolism

Hypothyroidism and Carotenemia

The well-known failure of hypothyroid patients to convert carotene to vitamin A is apparently related to fat level of the blood. In 25 cases chiefly due to cretinism or myxedema, Dr. Hugh W. Josephs of Johns Hopkins University, Baltimore, observed consistently high values of total serum lipid, cholesterol, and carotene, with relatively greater amounts of carotene. When thyroid medication is withdrawn or begun, the rise or fall of blood carotene lags behind that of total fat. Carotene probably depends on lipids not only for storage but also for absorption from the intestines and transport in the circulation.

Pediatrics 41:784-802, 1952.

Pathology

Splenic Influence

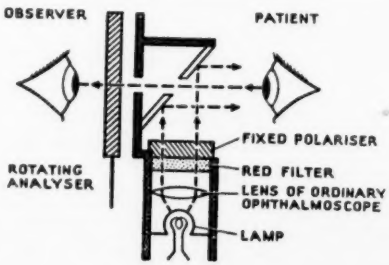
Continued intraperitoneal administration of methyl cellulose to rats produces a syndrome analogous to the condition known in man as secondary hypersplenism. The syndrome is characterized by splenomegaly, hyperplasia of the bone marrow, normocytic, normochromic anemia, leukopenia, and slight thrombocytopenia. In man, the hematologic abnormalities are alleviated by splenectomy though the underlying disease process is not changed. In the rat, previous splenectomy prevents the development of the hemopoietic disorders caused by methyl cellulose injections, but does not alter the histopathologic effects of the drug on spleen, liver, and kidney, report Dr. J. G. Palmer and associates of the University of Utah, Salt Lake City.

Blood 8:72-80, 1953.

Diabetes

Rapid Blood Sugar Test

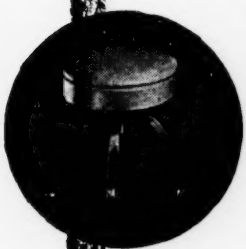
Alteration of the refraction of the eye effected by quantitative changes in blood sugar is the basis for a method for rapid estimation of circulating dextrose. Using an ophthalmoscope fitted with two polaroid screens, one movable over a scale, and a monochromatic light filter to give a sharp cut-off, Dr. D. W. Vere of the London Hospital obtains an approximation within ± 20 mg. per 100 mg. per 100 cc. of the laboratory finding by the Folin-Wu technic (see illustration).



The reading, requiring forty-five seconds to complete, is taken from the analyzer rotation and a calibration curve after corrections have been made for diffusion rate of dextrose, pupil size, and refractive error. An alternative but less accurate device substitutes neutral graded wedges for the polarizing element.

Lancet 263:1017, 1952.

Treat your patients on this new ROYAL HYDRAULIC CHAIR



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Apparatus

Hubless Needle for Venipuncture

An easily applied hubless needle for intravenous therapy comprises two needles, a No. 23 inserted into a No. 19, soldered to malleable copper sheeting. The flexible element may be bent to fit the contour of an infant's head or the dorsal finger vein of an older person. To use, Lt. Arthur S. Rathkey, M.C., U.S.A.F., of Hill Air Force Base Hospital, Ogden, Utah, attaches the device to polyethylene tubing with an internal diameter of 1 mm. connected to standard injection equipment by a conventional No. 19 needle. A single piece of tape across the base and skin holds the assembly securely.

New England J. Med. 247:985, 1952.

Anesthesiology

Antiarrhythmic Drug

Incidence and severity of cardiac arrhythmias occurring during anesthesia may be reduced by premedication with procaine amide. This drug has been evaluated in over 5,000 patients receiving various types of general anesthesia and has been found effective therapeutically as well as in prophylaxis. Adult dosage is 500 mg. of procaine amide given orally at the same time as other preanesthetic medication. Children receive the drug hypodermically as procaine amide gluconate in proportionately smaller doses. Dr. Charles L. Burstein of the Hospital for Special Surgery, New York City, cautions that procaine amide will not prevent hypoxic arrhythmias resulting from anesthetic mismanagement. Greatest efficacy is in preventing arrhythmias occasioned by sensitization of the cardiac conducting mechanism from the inhalant anesthetic. With procaine amide, surgery for the cardiac patient is less hazardous since digitalis need not be discontinued. Evidence also suggests that stimulatory arrhythmias that originate during endotracheal intubation and in other thoracic procedures may be obviated with procaine amide.

Anesthesiology 13:510-517, 1952.

Radioisotopes

Labeled Protein in Diagnosis

Pancreatic insufficiency may be diagnosed by measuring the fecal and urinary excretion of isotope by patients fed test meals containing I^{131}-labeled protein. The basis of the method used by Austin B. Chinn, M.D., and associates of Western Reserve University, Cleveland, is the diminution of intestinal hydrolysis of protein accompanying functional glandular deficiency. None of 11 persons without gastrointestinal disease excreted more than 4.8% of the ingested I^{131}, but each of 5 subjects with impaired function lost more than 5 times this amount. Administration of pancreatic extract with the meal decreased the amount of radioactive substance in the feces and increased the quantity in the urine of 3 of the patients with pancreatic insufficiency.

New England J. Med. 247:877-880, 1952.

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Highly effective in a wide range of bacterial, rickettsial, and viral pneumonias, CHLOROMYCETIN (chloramphenicol, Parke-Davis) is particularly valuable in mixed infections and where the causative agent is not easily ascertained.

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Chloromycetin (chloramphenicol, Parke-Davis) is available in a variety of forms, including: Chloromycetin Kapseals,® 250 mg., bottles of 16 and 100. Chloromycetin Capsules, 100 mg., bottles of 25 and 100. Chloromycetin Capsules, 50 mg., bottles of 25 and 100. Chloromycetin Ophthalmic Ointment, 1%, ⅛-ounce collapsible tubes. Chloromycetin Ophthalmic, 25 mg. dry powder for solution, individual vials with droppers.

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DETROIT, MICHIGAN

Treatment

Acute Pulmonary Edema

Nebulized 2-ethylhexanol administered with oxygen from a positive-pressure apparatus is apparently most effective in treatment of acute pulmonary edema. The drug, a synthetic antifoaming agent related to caprylic alcohol, is from 4 to 9 times as rapid-acting as ethyl alcohol. Dr. Nathaniel E. Reich and associates of the State University of New York, New York City, and Kings County Hospital, Brooklyn, suggest the following method: Insert 1/120 gr. of nitroglycerin under the tongue of the patient placed in a sitting position; repeat in ten minutes. With a closely fitting mask, administer oxygen bubbled through the medicament in a humidifier. If relief is not pronounced within fifteen minutes, slowly inject intravenously ⅛ gr. of morphine, taking not less than sixty seconds for the injection. If digitalis has not been used, slowly give 0.3 mg. of ouabain intravenously. When recovery is evident, intramuscular injection of a mercurial diuretic should be made and inhalation medication discontinued. Most of 14 patients with heart disease or toxic pneumonitis thus treated were relieved.

New York State J. Med. 52:2647-2648, 1952.

Meetings

X-Ray Technicians

The American Society of X-Ray Technicians and the Canadian Society of Radiological Technicians will hold a joint convention at Toronto, June 28 to July 2.

"Eunuchism has nothing to do with being 'cut out for the job.'"

Life's Weary Moments

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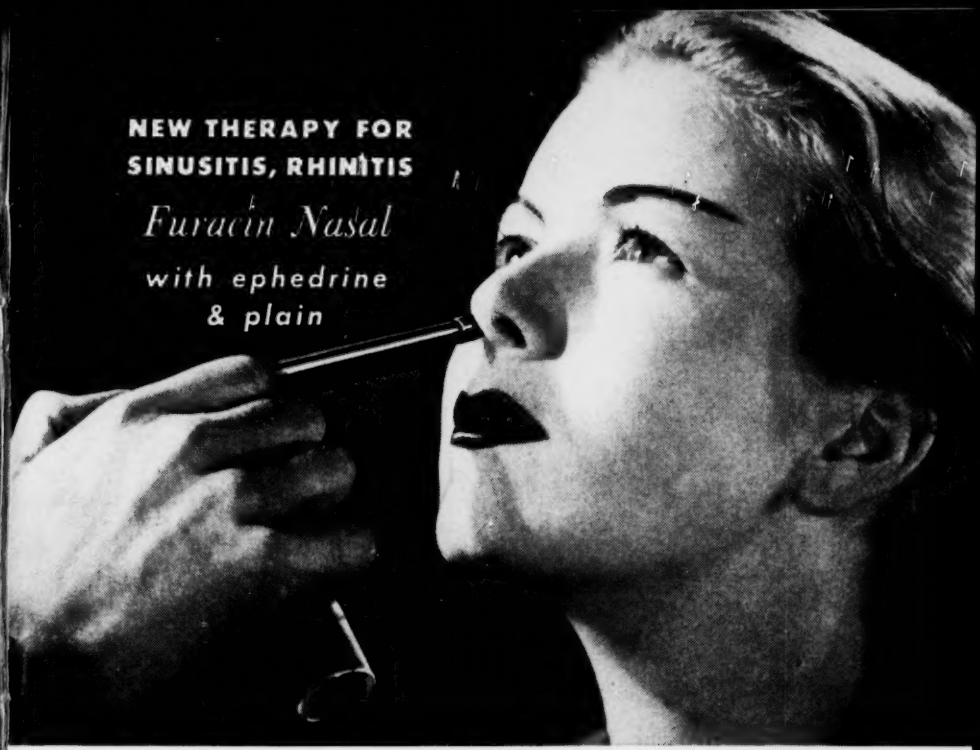

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Even those notoriously refractory conditions: atrophic rhinitis and ozena* show marked benefits from Furacin therapy.

* Thornell, W. C.: Arch. Otolaryng. 52:96 (July) 1950.

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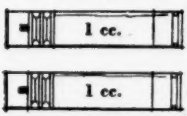

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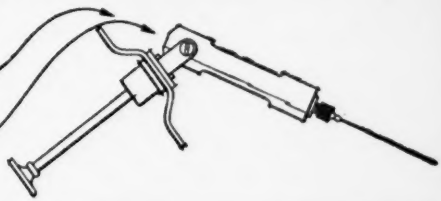

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Oncology

Proteinimine and Cancer

The protein-bound leukopenic activity of proteinimine is useful in treatment for acute leukemias, collagen diseases, and carcinomas of childhood. Dr. M. J. Brennan and associates of the Henry Ford Hospital, Detroit, find this compound, formed by the reaction of plasma with nitrogen mustard in vitro, less toxic and more extensively applicable than the parent substance. Essentially similar results are obtained with Hodgkin's disease, lymphosarcoma, periarteritis nodosum, and lupus erythematosus disseminatus whether nitrogen mustard or proteinimine is used.

Urology

Cortisone in Urethral Stricture

Strictures of the male urethra may respond favorably to cortisone therapy. After the hospitalized patient has had 3 daily intramuscular injections of 400,000 units of procaine penicillin, Dr. John E. Byrne of St. Louis University, St. Louis, dilates the urethra under spinal or intravenous barbiturate anesthesia until a 20F Kollman dilator can be placed so that the cicatricial tissue can be expanded to 30F. A 24F Foley type of catheter replaces the instrument and is retained for three days. Cortone is administered, 300 mg. in the first twenty-four hours after admission and then in 4 divided doses totaling 100 mg. daily for thirty days. A soluble sulfa compound is given during hormonal treatment to prevent secondary infection. Of 31 strictures of inflammatory and traumatic origin, 17 were still expanded as long as nine months later. The effect of the drug probably results from suppression or inhibition of the cellular enzyme systems, typical of the action of 11-oxygenated adrenocortical steroids in delaying fibroblastic and endothelial response.

Missouri Med. 50:23-27, 1953.

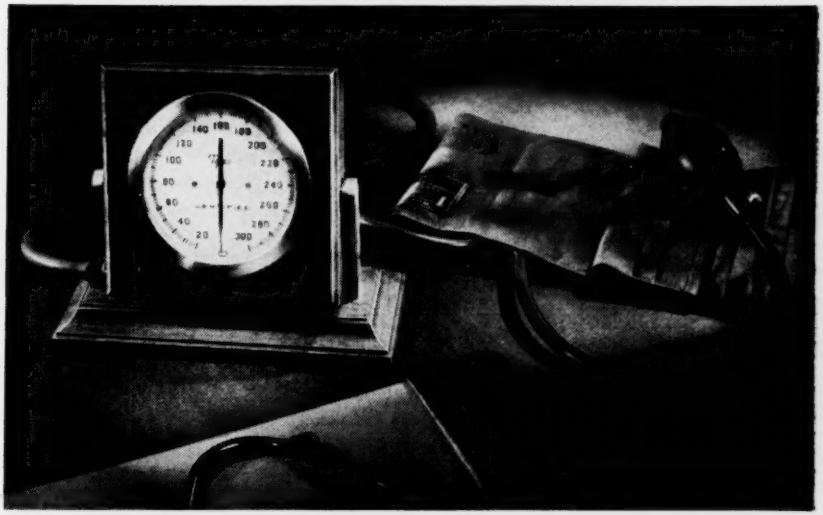
Gastroenterology

Antibiotics and Moniliasis

Overgrowth of intestinal fungi during antibiotic therapy probably results from the removal of coliform organisms, which naturally have a suppressive influence, rather than from direct stimulation by the drugs. Feeding of intestinal bacteria may be the most rapid method of eliminating moniliasis, observes Dr. Thomas Fite Paine, Jr., of Harvard University, Boston. In vitro, aureomycin, penicillin, or other antibacterial agent does not appreciably increase growth of typical strains of *Monilia* and yeast and often even suppresses such growth. But when coliform or mixed stool organisms and fungi are inoculated into the same flask, the antibiotic interferes with growth of the former and allows the fungi to flourish. Overabundant fungi in the bowel probably usurp B vitamins and may cause a deficiency in the human host, yet administration of a vitamin supplement would merely encourage the multiplication of the fungi.

Antibiot. & Chemother. 2:653-658, 1952.

New Tycos® Aneroid has DESKSIDE MANNER



There's no law that says sphygs can't be beautiful, as well as accurate and dependable. That's what we had in mind when we designed this new Tycos Desk Aneroid. The case is solid walnut, hand rubbed to a velvet finish, with satin brass finished trim. The 3⅜" ivory-tinted dial is easy to read, and the easel adjusts to any desired angle. The long pointer magnifies slight variations in the pulse wave, gives you maximum sensitivity.

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Experimental Surgery

Survival of Homografts

The life of full-thickness skin homografts in rabbits is prolonged 62% by streptokinase and streptodornase injected under the transplant. Untreated grafts have an inflammatory reaction five to seven days after transplantation, and by the tenth to fifteenth day are usually dry, hard, and black. Enzymes delay inflammation until the seventh to twelfth day. Drs. C. D. Dukes and T. G. Blocker, Jr., of the University of Texas, Galveston, believe that an antigen-antibody reaction takes place in the vessels supplying nutrition for the grafted tissue. Vascular endothelium is irritated, the walls dilate, and exudation, hemorrhage, and stagnation result. Apparently the same immunologic reactions occur in man, for example, in the Arthus phenomenon, which destroys tissue chiefly through vascular damage.

Ann. Surg. 136:999-1006, 1952.

Vital Statistics

Syphilis and Longevity

Nonsyphilitic persons live longer than syphilitic, according to vital statistics and clinical studies. Syphilis probably weakens resistance to other mortal diseases, remarks Dr. Paul D. Rosahn of New Britain, Conn., who finds that longevity in mice as well as in human beings is adversely affected by syphilitic infection but that death is not usually the direct consequence of the disease.

Arch. Dermat. & Syph. 66:547-568, 1952.

Doctor to Doctor

Think of a gag that fits the illustration. For every issue a new gag is published and the author is sent $5. The March 15 winner is

Lionel Goitein, M.D.
New York City

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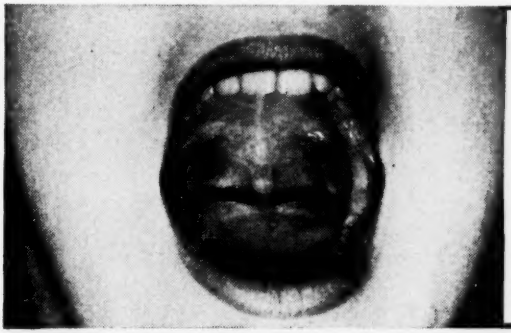

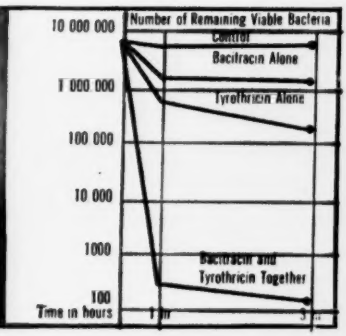

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Use of these potent, topical antibiotics obviates the danger of sensitizing the patient to antibiotics that are usually employed for systemic effect.

Antibiotics

Oral Penicillin

When given in conjunction with Benemid, oral penicillin maintains plasma concentrations equal to those procured with intramuscularly injected procaine penicillin. Dr. William P. Boger and associates of Norristown State Hospital, Norristown, Pa., report that Benemid acts by retarding renal elimination of penicillin. An initial oral dose of 400,000 units of potassium penicillin G combined with 1 gm. of Benemid results in a peak concentration of 1 to 2 units per cubic centimeter. Subsequent doses of 300,000 units of penicillin with 0.75 gm. of Benemid at eight-hour intervals result in peaks approximating 1 unit per cubic centimeter.

Antibiot. & Chemother. 2:555-562, 1952.

Hematology

ACTH and Cortisone for Blood Dyscrasias

Severe hypersensitive blood abnormalities as well as other manifestations of drug sensitivity may be treated by corticotropin or cortisone. Rapid recovery in 2 cases of agranulocytosis occurring in conjunction with thiosemicarbazone therapy for rheumatoid arthritis is reported by Dr. Mikko Virkkunen of the Kivelä Hospital, Helsinki. One patient received 250 mg. of ACTH in four days; the other, 40 mg. on the first day and 80 mg. on the second. Complete remission of thrombocytopenic purpura developing in an arthritic patient after the administration of gold salts was effected only after 585 mg. of corticotropin had been given in daily amounts of 30 to 60 mg. for two weeks, followed by 100 mg. daily for two weeks. A similar case required two courses of treatment with cortisone, 300 mg. on the first day, 200 mg. on the second day, and then 100 mg. daily for a total of 1.7 gm. in fifteen days, and subsequently an additional 3.4 gm. in forty days. The delayed recovery was probably caused by the slow excretion of the gold.

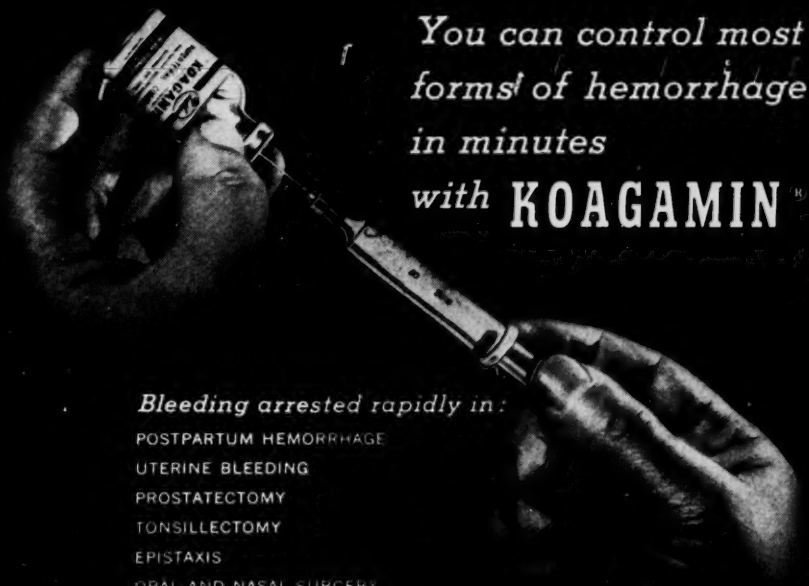
Arch. Int. Med. 90:580-586, 1952.

Gastroenterology

Antroduodenectomy for Duodenal Ulcer

The resection of chronic relapsing duodenal ulcer by antroduodenectomy and gastroduodenostomy maintains gastrointestinal continuity and leaves a capacious stomach. Two months after operation, Dr. Grayton Brown and associates of the Royal Melbourne Hospital and the Walter and Eliza Hall Institute of Medical Research, Melbourne, Australia, administer deep roentgen irradiation to reduce secretion of acid and pepsin for a period of six to nine months. The roentgen dose totals 2,000 r in three weeks. Of 10 patients thus treated, 9 had no symptoms and 1 had slight dyspepsia as long as seven months later. Neither postoperative medication nor diet is necessary with this scheme of treatment, but enough time has not elapsed for significant comparison with other methods.

Lancet 263:1145-1149, 1952.



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Washington Letter

(Continued from page 66)

abled, for example, money that was allocated for the blind. State officials feel that they should have this right.

Sen. Taft and a number of other leaders in this Congress hope somehow to put a brake on the number of federal dollars collected in taxes from the states, then passed back to them with instructions on how the money should be used. They argue that there isn't much logic in collecting the money in the first place, if it's certain to go back. Why not keep both money and responsibility closer to the people?

How far and how fast this philosophy can be translated into legislative action is uncertain, considering the massive and complicated interworkings of state and federal health and welfare programs. But there would be little to interfere with a simple change in some regulations—action that could be initiated by Mrs. Hobby to withdraw gradually any excessive federal control, without stopping the flow of dollars.

If any progress is made in this direction—and the effort definitely will be made—state officials will have a freer hand to use federal grants as they see fit. And doctors in turn will have fewer and fewer forms to make out, and fewer and fewer regulations to observe.

Also within the province of the new FSA administrator is the problem of what action to recommend to Congress on the highly controversial permanent and total disability section of the Social Security bill passed last session.

The section would waive payment of federal old age and survivors insurance premiums by workers found to be totally and permanently disabled, so that when they finally collected their old age pension the checks wouldn't be reduced because of the years they weren't able to work. Although the section is in the law, it can't become operative unless and until Congress passes enabling legislation.

American Medical Association fought the section last year, arguing that it gave the federal government too much control over the doctors who would have to make the determinations of disability. As a compromise, Dr. Louis H. Bauer now proposes that the examinations not be taken into account and that the pension check be based instead on the worker's best five or ten income years. But social security experts don't like this simplified solution, contending that it would be unfair to the worker who paid OASI premiums for say forty years.

Mrs. Hobby will find herself right in the middle of this argument, too.

The Doctor Draft

There is one piece of legislation of prime interest to doctors that does not involve the FSA administrator—the question of extending

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A-2448 Physicians Outfit for the Wintrobe Blood Sedimentation Test, including equipment listed above, complete with directions, each $14.50

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the doctor draft law. Action will have to be taken on this within the next few months or, the military services contend, they just cannot operate their medical departments.

At this writing, Defense Department is still trying to get together with American Medical Association and the American Dental Association on a compromise bill. The associations haven't said they won't support an extension, but they are using all possible pressure to make the military show that uniformed physicians are being used efficiently and that not too many civilian dependents are receiving medical care from military doctors.

However, indications still are that the law will be extended, with several changes: [1] a lowering of the maximum service age from 51 to probably 41 or 45, [2] separation of physicians into two groups, those with military service and those without, [3] provision for calling nonveterans first, then veterans, with those showing the least service called first.

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Louisville

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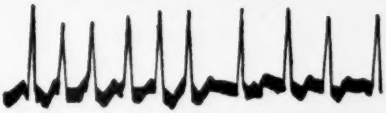
"It is the distal end of the bone, Miss Roe, not the dismal end."

to avoid up

and down



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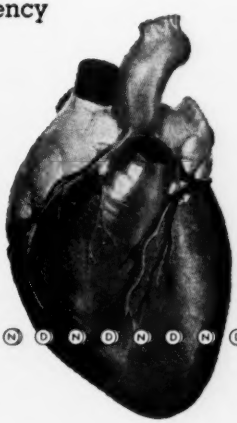

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Correspondence

(Continued from page 33)

low-grade fever of long duration. In the presence of such clinical and laboratory response the assumption is strengthened that *Brucella* infection or allergy is responsible for the patient's symptoms. No conclusive diagnosis can be made on such a basis, however.

• A negative skin test has great value in ruling out brucellosis in approximately 95% of chronic cases. Rarely the skin test is negative in the presence of agglutinins in high titer, complement fixation, or positive culture. The skin test is never used in cases where only recent infection is suspected since skin allergy does not develop early. Even a negative skin test may stimulate agglutinin, opsonin, and complement response. Skin testing is of no value in the acute febrile illness because of possible nondevelopment of cutaneous allergy and because severe exacerbations of the illness may be precipitated. Agglutination and complement-fixation reactions and/or culture alone are adequate in the acute febrile illness.

• The great majority of patients showing significant phagocytosis of *Brucella*, agglutinins in low titer, or positive complement-fixation reaction and positive skin test respond in a characteristic manner to therapeutic test doses of *Br. abortus* vaccine given in subtolerant, nonshock-producing doses. This clinical and serologic response is not duplicated by nonspecific foreign protein such as intravenous typhoid vaccine.

• Of some additional diagnostic value is the finding of leukopenia with or without relative lymphocytosis and normal sedimentation rates. Anemia, not always microcytic, is frequent and occasionally marked eosinophilia is present.

• In the presence of clinical and/or psychologic test evidence of neurosis or symptoms common to brucellosis or neurosis, such as anxiety, depression, and sexual inadequacy, differentiation may be extremely difficult. In some patients direct correlation between *Brucella* infection and neuropsychiatric conditions must be seriously considered.

Assessment of various noncultural tests for brucellosis is not possible except through application of these tests in large numbers of patients observed over long periods of time. The accuracy of the clinical-laboratory approach described has been demonstrated during a period of twenty-one years through the diagnosis and treatment of more than 800 patients, about 95% of whom were in the chronic phase of brucellosis.

In the past seven years the addition of psychiatric examination and psychologic testing has resulted in greater diagnostic accuracy and consequently in better therapeutic results. The percentage of error need be no greater than that in atypical rheumatic fever or other diseases in which cultural proof or other definitive diagnostic procedure is lacking.

HAROLD J. HARRIS, M.D.
New York City

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EMERGENCIES IN MEDICAL PRACTICE *edited by* C. Allan Birch. 3d ed. 587 pp., ill. E. & S. Livingstone, Edinburgh. 32*s*. 6*d*.

AN INTRODUCTION TO MEDICAL SCIENCE: AN ELEMENTARY TEXT ON PATHOLOGY *by* William Boyd. 4th ed. 304 pp., ill. Lea & Febiger, Philadelphia. $4.50

THE HARVEY LECTURES *by* Dr. W. T. Astbury *et al.* Series 46, 1950-51. 314 pp., ill. Charles C Thomas, Springfield, Ill. $8.75

Cardiovascular Diseases

CARDIOGRAPHIC TECHNIQUE: MANUAL FOR CARDIOLOGICAL TECHNICIANS *by* S. L. Barron *and* A. Schott. 156 pp., ill. Grune & Stratton, New York City. $4.50

DISEASES OF THE HEART AND ARTERIES *by* George R. Herrmann. 4th ed. 652 pp., ill. C. V. Mosby Co., St. Louis. $12.50

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NEUROSURGERY IN GENERAL PRACTICE *by* Adrien Henri Ver Brugghen. 687 pp., ill. Charles C Thomas, Springfield, Ill. $14

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OCULAR SURGERY *by* H. Arruga; *translated by* Michael J. Hogan *and* Luis E. Chaparro. 936 pp., ill. McGraw-Hill Book Co., New York City. $36

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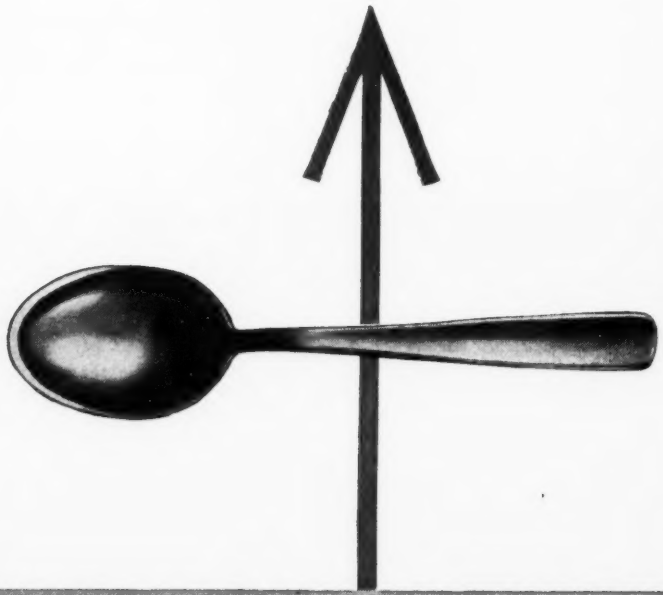

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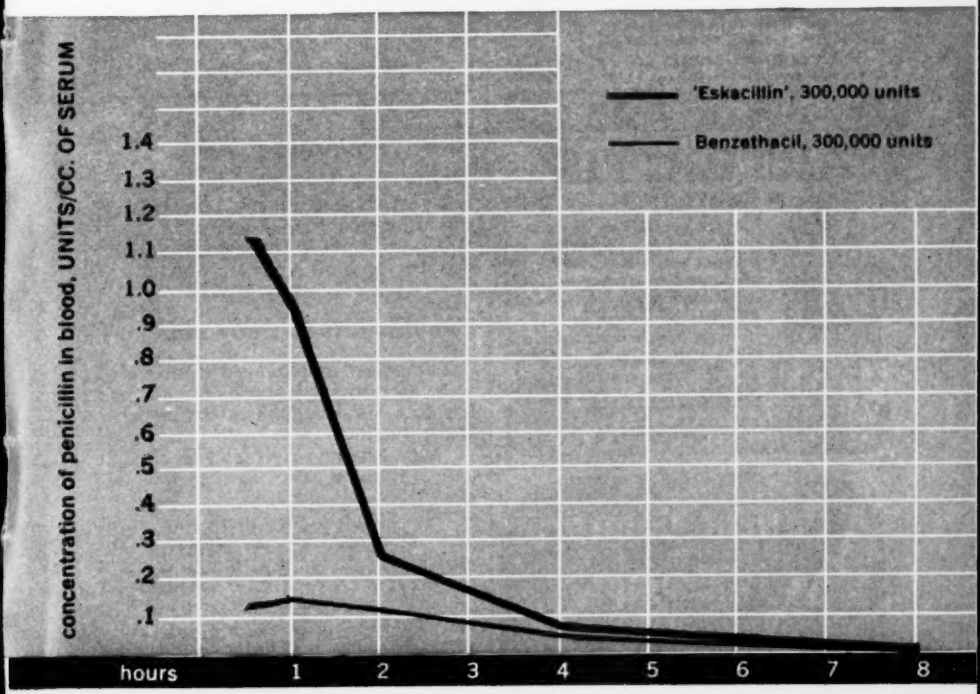

Source: Foltz, E.L., and Schimmel, N.H.: Antibiotics & Chemotherapy, to be published.

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'Eskacillin 100'	100,000 units potassium penicillin G
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"No, no, Doctor, that's not it at all. You see, all my children are grown up. I am not going to mind the pregnancy, or even the delivery, I am sure. And it will be fun to have a baby in the house again. But pretty soon, that baby will grow up to school age and then there will be PTA again. Doctor, I just never, never could go through with that again!"—R.H.

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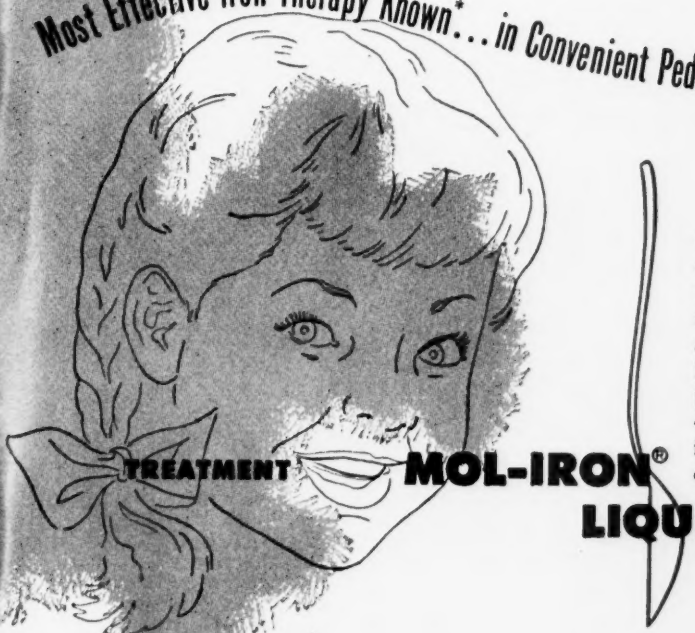

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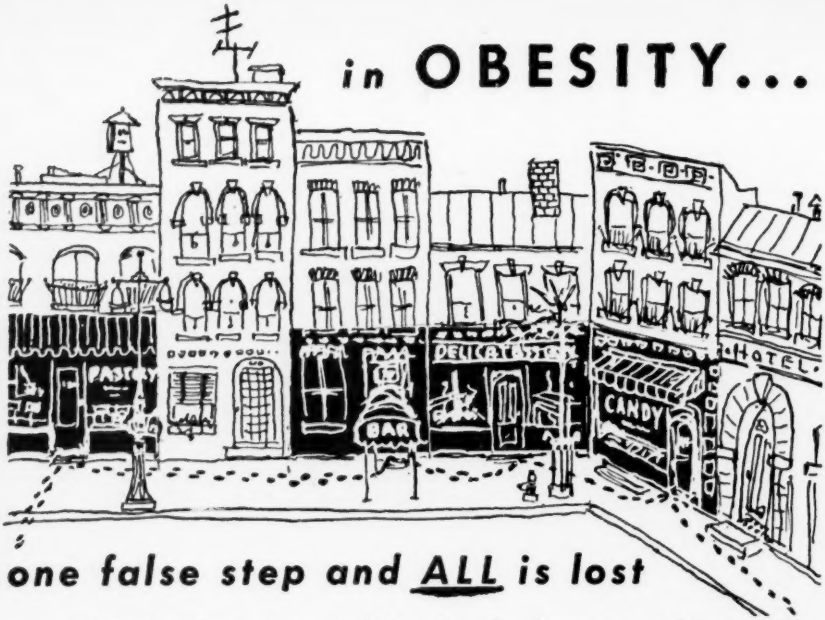

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When five cubic centimeters of RAMSES* Vaginal Jelly† are deposited against the cervical os, as shown in the above illustration, it is hardly possible for sperm either to penetrate the barrier that is formed or to escape its spermatocidal action.

Continuing studies conducted by independent accredited laboratories establish both the occlusive and spermatocidal efficiency of RAMSES Vaginal Jelly. Physicians can prescribe this dependable contraceptive with complete assurance.

†Active ingredients, by weight: dodecaethyleneglycol monolaurate 5%; boric acid 1%; alcohol 5%.

*The word RAMSES is a registered trademark of Julius Schmid, Inc.

gynecological division

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